	0.1.00.1.5.4440/PTO			Complete if Known		
Substitute for 1449/PTO				Application Number	10/701,007	
INFORMATION DISCLOSURE				Filing Date	November 4, 2003	
STATEMENT BY APPLICANT			CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet	1	of	56	Attorney Docket Number	ISIS-5325	

	U. S. PATENT DOCUMENTS						
Examiner Initials	Cite No.	Document Number Number – Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear		
	1	2002/0049173 A1	04-25-2002	Bennett et al.			
	2	2002/0068708 A1	06-06-2002	Wengel et al.			
	3	2002/0071826 A1	06-13-2002	Tamarkin et al.			
	4	2002/0081577 A1	06-27-2002	Kilkuskie et al.			
	5	2002/0102267 A1	08-01-2002	Lu et al.			
	6	2002/0147332 A1	10-10-2002	Kaneko			
	7	2002/0156235 A1	10-24-2002	Manoharan et al.			
	8	2002/0162126 A1	10-30-2002	Beach et al.			
	9	2002/0165189 A1	11-07-2002	Crooke			
	10	2002/1051512 A1	10-17-2002	Peyman et al.			
	11	2003/0004325 A1	01-02-2003	Cook et al.			
	12	2003/0027780 A1	02-06-2003	Hardee et al.			
	13	2003/0096286 A1	05-22-2003	Crooke			
	14	2003/0096287 A1	05-22-2003	Crooke			
	15	2003/0096784 A1	05-22-2003	Crooke			
	16	2003/0119777 A1	06-26-2003	Crooke			
	17	2003/0125241 A1	07-03-2003	Wissenbach et al.			
	18	2003/0139585 A1	07-24-2003	Uhlmann et al.			
	19	2003/0158403 A1	08-21-2003	Manoharan et al.			
	20	2003/0166282 A1	09-04-2003	Brown et al.			
	21	2003/0175906 A1	09-18-2003	Manoharan et al.			
	22	2003/0187240 A1	10-02-2003	Cook et al.			
	23	2003/0190635 A1	10-09-2003	McSwiggen			
	24	2003/0207804 A1	11-06-2003	Manoharan et al.			
	25	2003/0224377 A1	12-04-2003	Wengel et al.			
	26	2004/0001811 A1	01-01-2004	Kreutzer et al.			

Examiner	Date	
Signature	Considered	

Substitute for 1449/PTO				Complete if Known		
				Application Number	10/701,007	
INFORMATION DISCLOSURE				Filing Date	November 4, 2003	
STATEMENT BY APPLICANT  (use as many sheets as necessary)			CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
				Examiner Name	Jane J. Zara	
Sheet	2	of	56	Attorney Docket Number	ISIS-5325	

	U. S. PATENT DOCUMENTS						
Examiner Initials	Cite No.	Document Number Number – Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear		
	27	2004/0009938 A1	01-15-2004	Manoharan et al.			
	28	2004/0014957 A1	01-22-2004	Eldrup et al.			
	29	2004/0029275 A1	02-12-2004	Brown et al.			
	30	2004/0102618 A1	05-27-2004	Crooke et al.			
	31	2004/0146867 A1	07-29-2004	Slattum et al.			
	32	2004/0171033 A1	09-02-2004	Baker et al.			
	33	2004/0259247 A1	12-23-2004	Tuschl et al.			
	34	2005/0020525 A1	01-27-2005	McSwiggen et al.			
	35	2005/0080246 A1	04-14-2005	Allerson et al.			
	36	2005/0164209 A1	07-28-2005	Bennett et al.			
	37	2005/0181382 A1	08-18-2005	Zamore et al.			
	38	2005/0221275 A1	10-06-2005	Bennett et al.			
	39	2005/0245474 A1	11-03-2005	Baker et al.			
	40	2005/0273868 A1	12-08-2005	Rana			
	41	2006/0127891 A1	06-15-2006	McSwiggen et al.			
	42	2007/0032446 A1	02-08-2007	Cook et al.			
	43	4,373,071	02-08-1983	Itakura			
	44	4,381,344	04-26-1983	Rideout et al.			
	45	4,401,796	08-30-1983	Itakura			
	46	4,415,732	11-15-1983	Caruthers et al.			
	47	4,426,330	01-17-1984	Sears			
	48	4,458,066	07-03-1984	Caruthers et al.			
	49	4,469,863	09-04-1984	Ts'o et al.			
	50	4,476,301	10-09-1954	Imbach et al.			
	51	4,500,707	02-19-1985	Caruthers et al.			
	52	4,507,433	03-26-1985	Miller et al.			

Examiner	Date	
Signature	Considered	

	0   1   1   1   1   1   1   1   1   1			Complete if Known		
Substitute for 1449/PTO				Application Number	10/701,007	
INFORMATION DISCLOSURE				Filing Date	November 4, 2003	
STA <sup>-</sup>	STATEMENT BY APPLICANT			First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet	3	of	56	Attorney Docket Number	ISIS-5325	

	U. S. PATENT DOCUMENTS						
Examiner Initials	Cite No.	Document Number Number – Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear		
	53	4,511,713	04-16-1985	Miller et al.			
	54	4,534,899	08-13-1985	Sears			
	55	4,587,044	05-06-1986	Miller			
	56	4,605,735	08-12-1986	Miyoshi			
	57	4,667,025	05-19-1987	Miyoshi			
	58	4,668,777	05-26-1987	Caruthers et al.			
	59	4,689,320	08-25-1987	Kaji			
	60	4,720,483 A	01-19-1988	Jansz et al.			
	61	4,725,677	02-16-1988	Koster et al.			
	62	4,757,141	07-12-1988	Fung et al.			
	63	4,760,017	07-26-1988	McCormick			
	64	4,762,779	08-09-1988	Snitman			
	65	4,789,737	12-06-1988	Miyoshi			
	66	4,812,512	03-14-1989	Buendia et al.			
	67	4,824,941	04-25-1989	Gordon			
	68	4,828,979	05-09-1989	Klevan			
	69	4,835,263	05-30-1989	Nguyen			
	70	4,845,205	07-04-1989	Huynh Dinh et al.			
	71	4,849,320	07-18-1989	Irving et al.			
	72	4,849,513	07-18-1989	Smith et al.			
	73	4,876,335	10-24-1989	Yamane			
	74	4,904,582	02-27-1990	Tullis			
	75	4,908,405	03-13-1990	Bayer et al.			
	76	4,924,624	05-15-1990	Suhadolnik et al.			
	77	4,948,882	08-14-1990	Ruth			
	78	4,958,013	09-18-1990	Letsinger			

Examiner	Date	
Signature	Considered	

Substitute for 1449/PTO				Complete if Known		
				Application Number	10/701,007	
INFORMATION DISCLOSURE				Filing Date	November 4, 2003	
STATEMENT BY APPLICANT  (use as many sheets as necessary)			CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
				Examiner Name	Jane J. Zara	
Sheet	4	of	56	Attorney Docket Number	ISIS-5325	

	U. S. PATENT DOCUMENTS						
Examiner Initials	Cite No.	Document Number Number – Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear		
	79	4,965,350	10-23-1990	Inoue et al.			
	80	4,973,679	11-27-1990	Caruthers et al.			
	81	5,013,556	05-07-1991	Woodle et al.			
	82	5,023,243	06-11-1991	Tullis			
	83	5,082,830	01-21-1992	Brakel			
	84	5,082,934	01-21-1992	Saba et al.			
	85	5,108,921	04-28-1992	Low et al.			
	86	5,109,124	04-28-1992	Ramathandran			
	87	5,112,963	05-12-1992	Pieles			
	88	5,118,802	06-02-1992	Smith			
	89	5,130,302	07-14-1992	Spielvogel et al.			
	90	5,132,418	07-21-1992	Caruthers et al.			
	91	5,134,066	07-28-1992	Rogers et al.			
	92	5,138,045	08-11-1992	Cook			
	93	5,142,047 A	08-25-1992	Summerton et al.			
	94	5,149,782 A	09-22-1992	Chang et al.			
	95	5,151,510	09-29-1992	Stec et al.			
	96	5,175,273	12-29-1992	Bischofberger et al.			
	97	5,177,196	01-05-1993	Meyer, Jr. et al.			
	98	5,177,198	01-05-1993	Spielvogel et al.			
	99	5,188,897	02-23-1993	Suhadolnik et al.			
	100	5,194,599	03-16-1993	Froehler et al.			
	101	5,212,295 A	05-18-1993	Cook			
	102	5,213,804	05-25-1993	Martin et al.			
	103	5,214,135 A	05-25-1993	Srivastava et al.			
	104	5,214,136	05-25-1993	Lin			

Examiner	Date	
Signature	Considered	

Out of the to for AAAO/DTO				Complete if Known		
Substitute for 1449/PTO				Application Number	10/701,007	
INFORMATION DISCLOSURE				Filing Date	November 4, 2003	
STA	LEMENT E	BY APPLIC	CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet	5	of	56	Attorney Docket Number	ISIS-5325	

		U. S	. PATENT DOC	UMENTS	
Examiner Initials	Cite No.	Document Number Number – Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines Where Relevant Passages or Relevan Figures Appear
	105	5,218,105	06-08-1993	Cook	
	106	5,227,170	07-13-1993	Sullivan	
	107	5,245,022	09-14-1993	Weis	
	108	5,254,469	10-19-1993	Warren	
	109	5,258,506	11-02-1993	Urdea	
	110	5,262,536	11-16-1993	Hobbs	
	111	5,264,221	11-23-1993	Tagawa et al.	
	112	5,264,423	11-23-1993	Cohen et al	
	113	5,272,250	12-21-1993	Spielvogel	
	114	5,276,019	01-04-1994	Cohen et al	
	115	5,278,302	01-11-1994	Caruthers et al.	
	116	5,286,717	02-15-1994	Cohen et al	
	117	5,292,873	03-08-1994	Rokita	
	118	5,317,098	05-31-1994	Shizuya	
	119	5,321,131	06-14-1994	Agrawal et al.	
	120	5,354,844	10-11-1994	Beug et al.	
	121	5,356,633	10-18-1994	Woodle et al.	
	122	5,367,066	11-22-1994	Urdea et al.	
	123	5,371,241	12-06-1994	Brush	
	124	5,378,825	01-03-1995	Cook et al.	
	125	5,386,023	01-31-1995	Sanghvi et al.	
	126	5,391,667	02-21-1995	Dellinger	
	127	5,391,723	02-21-1995	Priest	
	128	5,395,619	03-07-1995	Zalipsky et al.	
	129	5,399,676	03-21-1995	Froehler et al.	
	130	5,405,939	04-11-1995	Suhadolnik et al.	

Examiner	Date	
Signature	Considered	

Out of the form AAAO/DTO				Complete if Known		
Substitute for 1449/PTO				Application Number	10/701,007	
INFORMATION DISCLOSURE				Filing Date	November 4, 2003	
STA	LEMENT E	BY APPLIC	CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet	6	of	56	Attorney Docket Number	ISIS-5325	

	U. S. PATENT DOCUMENTS						
Examiner Initials	Cite No.	Document Number Number – Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear		
	131	5,414,077	05-09-1995	Lin			
	132	5,416,016	05-16-1995	Low et al.			
	133	5,416,203	05-16-1995	Letsinger			
	134	5,417,978	05-23-1995	Tari et al.			
	135	5,424,413	06-13-1995	Hogan et al.			
	136	5,432,272	07-11-1995	Benner			
	137	5,451,463	09-19-1995	Nelson			
	138	5,453,496	09-26-1995	Caruthers et al.			
	139	5,455,233	10-03-1995	Spielvogel et al.			
	140	5,457,187	10-10-1995	Gmeiner et al.			
	141	5,457,191	10-10-1995	Cook et al.			
	142	5,459,127	10-17-1995	Felgner et al.			
	143	5,459,255	10-17-1995	Cook et al.			
	144	5,462,854	10-31-1995	Coassin et al.			
	145	5,469,854	11-28-1995	Unger et al.			
	146	5,476,925	12-19-1995	Letsinger et al.			
	147	5,484,908	01-16-1996	Froehler et al.			
	148	5,486,603	01-23-1996	Bahr			
	149	5,502,177	03-26-1996	Matteucci et al.			
	150	5,506,212	04-09-1996	Hoke et al.			
	151	5,506,337	04-09-1996	Summerton et al.			
	152	5,506,351	04-09-1996	McGee			
	153	5,508,270	04-16-1996	Baxter et al.			
	154	5,510,475	04-23-1996	Agrawal			
	155	5,512,295	04-30-1996	Kornberg et al.			
	156	5,512,439	04-30-1996	Hornes			

Examiner	Date	
Signature	Considered	

Out of the form AAAO/DTO				Complete if Known		
Substitute for 1449/PTO				Application Number	10/701,007	
INFORMATION DISCLOSURE				Filing Date	November 4, 2003	
STA	TEMENT E	BY APPLIC	CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet	7	of	56	Attorney Docket Number	ISIS-5325	

	U. S. PATENT DOCUMENTS						
Examiner Initials	Cite No.	Document Number Number – Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear		
	157	5,512,667	04-30-1996	Reed			
	158	5,514,786	05-07-1996	Cook et al.			
	159	5,519,126	05-21-1996	Hecht			
	160	5,521,291	05-28-1996	Curiel et al.			
	161	5,525,465	06-11-1996	Haralambidis			
	162	5,525,711	06-11-1996	Hawkins et al.			
	163	5,527,528	06-18-1996	Allen et al.			
	164	5,527,899	06-18-1996	Froehler			
	165	5,532,130	07-02-1996	Alul			
	166	5,534,259	07-09-1996	Zalipsky et al.			
	167	5,536,821	07-16-1996	Agrawal et al.			
	168	5,539,082	07-23-1996	Nielsen et al.			
	169	5,539,083	07-23-1996	Cook et al.			
	170	5,541,306	07-30-1996	Agrawal et al.			
	171	5,541,313	07-30-1996	Ruth			
	172	5,543,152	08-06-1996	Webb et al.			
	173	5,543,158	08-06-1996	Gref et al.			
	174	5,545,730	08-13-1996	Urdea			
	175	5,547,932	08-20-1996	Curiel et al.			
	176	5,550,111	08-27-1996	Suhadolnik et al.			
	177	5,552,538	09-13-1996	Urdea			
	178	5,552,540	09-03-1996	Haralambidis			
	179	5,556,948	09-17-1996	Tagawa et al.			
	180	5,561,043	10-01-1996	Cantor et al.			
	181	5,563,253	10-08-1996	Agrawal et al.			
	182	5,565,552	10-15-1996	Magda			

Examiner	Date	
Signature	Considered	

0.1.614.6.4440/PTO				Complete if Known		
Substitute for 1	1449/PTO			Application Number	10/701,007	
		DISCLOS		Filing Date	November 4, 2003	
STA <sup>-</sup>	STATEMENT BY APPLICANT			First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet	8	of	56	Attorney Docket Number	ISIS-5325	

U. S. PATENT DOCUMENTS						
Examiner Initials	Cite No.	Document Number Number – Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	
	183	5,565,555	10-15-1996	Froehler et al.		
	184	5,567,810	10-22-1996	Weis		
	185	5,571,799	11-05-1996	Tkachuk et al.		
	186	5,574,142	11-12-1996	Meyer		
	187	5,576,302 A	11-19-1996	Cook et al.		
	188	5,578,717	11-26-1996	Urdea		
	189	5,578,718	11-26-1996	Cook		
	190	5,580,575	12-03-1996	Unger et al.		
	191	5,580,731	12-03-1996	Chang		
	192	5,582,188 A	12-10-1996	Benderev et al.		
	193	5,583,020	12-17-1996	Arnold, Jr. et al.		
	194	5,585,481	12-17-1996	Arnold		
	195	5,587,361	12-24-1996	Cook et al.		
	196	5,587,371	12-24-1996	Sessler		
	197	5,587,469	12-24-1996	Cook et al.		
	198	5,591,584	01-07-1997	Chang		
	199	5,591,721	01-07-1997	Agrawal et al.		
	200	5,594,121	01-14-1997	Froehler et al.		
	201	5,595,726	01-21-1997	Magda		
	202	5,595,756	01-21-1997	Bally et al.		
	203	5,596,091	01-21-1997	Switzer et al.		
	204	5,597,696	01-28-1997	Linn		
	205	5,599,797 A	02-04-1997	Cook et al.		
	206	5,599,923	02-04-1997	Sessler		
	207	5,599,925	02-04-1997	Torii		
	208	5,599,928	02-04-1997	Hemmi et al.		

Examiner	Date	
Signature	Considered	

0.1.65.4.6.4440/PTO				Complete if Known		
Substitute for 1449/PTO				Application Number	10/701,007	
		DISCLOS		Filing Date	November 4, 2003	
STATEMENT BY APPLICANT			CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet	9	of	56	Attorney Docket Number	ISIS-5325	

U. S. PATENT DOCUMENTS							
Examiner Initials	Cite No.	Document Number Number – Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear		
	209	5,607,923 A	03-04-1997	Cook et al.			
	210	5,612,469 A	03-18-1997	Goodchild			
	211	5,614,617	03-25-1997	Cook et al.			
	212	5,614,621	03-25-1997	Ravikumar et al.			
	213	5,625,050	04-29-1997	Beaton et al.			
	214	5,631,148	05-20-1997	Urdea			
	215	5,634,488 A	06-03-1997	Martin, Jr.			
	216	5,635,488 A	06-03-1997	Cook et al.			
	217	5,639,647 A	06-17-1997	Usman et al.			
	218	5,643,889 A	07-01-1997	Suhadolnik et al.			
	219	5,645,985	07-08-1997	Froehler et al.			
	220	5,658,731 A	08-19-1997	Sproat et al.			
	221	5,661,134 A	08-26-1997	Cook et al.			
	222	5,663,360 A	09-02-1997	Bortolaso et al.			
	223	5,672,662 A	09-30-1997	Harris et al.			
	224	5,672,695 A	09-30-1997	Eckstein et al.			
	225	5,672,697	09-30-1997	Buhr et al.			
	226	5,677,289 A	10-14-1997	Torrence et al.			
	227	5,681,941	10-28-1997	Cook et al.			
	228	5,684,142 A	11-04-1997	Mishra et al.			
	229	5,684,143 A	11-04-1997	Gryaznov et al.			
	230	5,684,243 A	11-04-1997	Gururaja et al.			
	231	5,688,941	11-18-1997	Cook			
	232	5,698,687 A	12-16-1997	Eckstein et al.			
	233	5,700,785 A	12-23-1997	Suhadolnik et al.			
	234	5,714,166 A	02-03-1998	Tomalia et al.			

Examiner	Date	
Signature	Considered	

Out of the to for AAAO/DTO				Complete if Known		
Substitute for 1449/PTO				Application Number	10/701,007	
		DISCLOS		Filing Date	November 4, 2003	
STATEMENT BY APPLICANT			CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet	10	of	56	Attorney Docket Number	ISIS-5325	

U. S. PATENT DOCUMENTS							
Examiner Initials	Cite No.	Document Number Number – Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear		
	235	5,714,331	02-03-1998	Buchardt et al.			
	236	5,716,824 A	02-10-1998	Beigelman et al.			
	237	5,719,262	02-17-1998	Buchardt et al.			
	238	5,719,271	02-17-1998	Cook et al.			
	239	5,721,218	02-24-1998	Froehler et al.			
	240	5,726,297 A	03-10-1998	Gryaznov et al.			
	241	5,750,666 A	05-12-1998	Caruthers et al.			
	242	5,750,669 A	05-12-1998	Rosch et al.			
	243	5,750,692	05-12-1998	Cook et al.			
	244	5,760,202	06-02-1998	Cook et al.			
	245	5,763,588	06-09-1998	Matteucci et al.			
	246	5,770,713	06-23-1998	Imbach et al.			
	247	5,770,716 A	06-23-1998	Khan et al.			
	248	5,777,092 A	07-07-1998	Cook et al.			
	249	5,789,576 A	08-04-1998	Daily et al.			
	250	5,792,844 A	08-11-1998	Sanghvi et al.			
	251	5,792,847 A	08-11-1998	Buhr et al.			
	252	5,801,154 A	09-01-1998	Baracchini et al.			
	253	5,804,683	09-08-1998	Usman et al.			
	254	5,808,023 A	09-15-1998	Sanghvi et al.			
	255	5,817,781 A	10-06-1998	Swaminathan et al.			
	256	5,830,635 A	11-03-1998	Agnello			
	257	5,830,653	11-03-1998	Froehler et al.			
	258	5,837,835 A	11-17-1998	Gryaznov et al.			
	259	5,837,852 A	11-17-1998	Chung et al.			
	260	5,840,876 A	11-24-1998	Beigelman et al.			

Examiner	Date	
Signature	Considered	

Out of the form 4.440/DTO				Complete if Known		
Substitute for 1449/PTO				Application Number	10/701,007	
	RMATION			Filing Date	November 4, 2003	
STA <sup>-</sup>	STATEMENT BY APPLICANT			First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet	11	of	56	Attorney Docket Number	ISIS-5325	

U. S. PATENT DOCUMENTS							
Examiner Initials	Cite No.	Document Number Number – Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear		
	261	5,859,221 A	01-12-1999	Cook et al.			
	262	5,861,493	01-19-1999	Cook et al.			
	263	5,872,232 A	02-16-1999	Cook et al.			
	264	5,874,553	02-23-1999	Peyman et al.			
	265	5,891,683	04-06-1999	Usman et al.			
	266	5,891,684	04-06-1999	Usman et al.			
	267	5,914,396 A	06-22-1999	Cook et al.			
	268	5,936,080 A	08-10-1999	Stec et al.			
	269	5,945,521 A	08-31-1999	Just et al.			
	270	5,962,425	10-05-1999	Walder et al.			
	271	5,965,720 A	10-12-1999	Gryaznov et al.			
	272	5,965,721 A	10-12-1999	Cook et al.			
	273	5,969,116 A	10-19-1999	Martin			
	274	5,969,118 A	10-19-1999	Sanghvi et al.			
	275	5,986,083 A	11-16-1999	Dwyer et al.			
	276	5,998,203	12-07-1999	Matulic-Adamic et al.			
	277	5,998,588 A	12-07-1999	Hoffman et al.			
	278	6,001,841	12-14-1999	Cook et al.			
	279	6,005,087	12-21-1999	Cook et al.			
	280	6,005,094 A	12-21-1999	Simon et al.			
	281	6,005,096	12-21-1999	Matteucci et al.			
	282	6,007,992	12-28-1999	Lin et al.			
	283	6,013,785 A	01-11-2000	Bruice et al.			
	284	6,015,886 A	01-18-2000	Dale et al.			
	285	6,020,475	02-01-2000	Capaldi et al.			
	286	6,025,140	02-15-2000	Langel et al.			

Examiner	Date	
Signature	Considered	

Out of the to for AAAO/DTO				Complete if Known		
Substitute for 1449/PTO				Application Number	10/701,007	
		DISCLOS		Filing Date	November 4, 2003	
STATEMENT BY APPLICANT			CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet	12	of	56	Attorney Docket Number	ISIS-5325	

U. S. PATENT DOCUMENTS							
Examiner Initials	Cite No.	Document Number Number – Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear		
	287	6,028,183	02-22-2000	Lin et al.			
	288	6,028,188 A	02-22-2000	Arnold, Jr. et al.			
	289	6,037,463	03-14-2000	Uhlmann et al.			
	290	6,043,060	03-28-2000	Imanishi			
	291	6,043,352 A	03-28-2000	Manoharan et al.			
	292	6,051,699	04-18-2000	Ravikumar			
	293	6,087,484 A	07-11-2000	Goodchild			
	294	6,096,875 A	08-01-2000	Khan et al.			
	295	6,111,085 A	08-29-2000	Cook et al.			
	296	6,117,657 A	09-12-2000	Usman et al.			
	297	6,121,437	09-19-2000	Guzaev et al.			
	298	6,127,346	10-03-2000	Peyman et al.			
	299	6,127,533 A	10-03-2000	Cook et al.			
	300	6,147,200	11-14-2000	Manoharan et al.			
	301	6,153,737 A	11-28-2000	Manoharan et al.			
	302	6,166,188 A	12-26-2000	Cook et al.			
	303	6,169,177	01-02-2001	Manoharan			
	304	6,172,208 B1	01-09-2001	Cook			
	305	6,172,216 B1	01-09-2001	Bennett et al.			
	306	6,207,646	03-27-2001	Krieg et al.			
	307	6,210,892 B1	04-03-2001	Bennett et al.			
	308	6,220,025 B1	04-24-2001	Mauti et al.			
	309	6,222,025 B1	04-24-2001	Cook et al.			
	310	6,227,982 B1	05-08-2001	Wurster			
	311	6,239,265 B1	05-29-2001	Cook			
	312	6,239,272 B1	05-29-2001	Beigelman et al.			

Examiner	Date	
Signature	Considered	

0.1.17.1.6.4440/DTO				Complete if Known		
Substitute for 7	Substitute for 1449/PTO			Application Number	10/701,007	
INFORMATION DISCLOSURE				Filing Date	November 4, 2003	
STA	LEMENT E	BY APPLIC	CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Jane J. Zara	
Sheet	13	of	56	Attorney Docket Number	ISIS-5325	

		U. S. I	PATENT DOC	UMENTS	
Examiner Initials	Cite No.	Document Number Number – Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	313	6,262,241 B1	07-17-2001	Cook et al.	
	314	6,268,490	07-31-2001	Imanishi et al.	
	315	6,274,723 B1	08-14-2001	Nilsen	
	316	6,277,634	08-21-2001	McCall et al.	
	317	6,277,967 B1	08-21-2001	Manoharan	
	318	6,281,201 B1	08-28-2001	Suhadolnik et al.	
	319	6,284,538 B1	09-04-2001	Monia et al.	
	320	6,287,860	09-11-2001	Monia et al.	
	321	6,300,319 B1	10-09-2001	Manoharan	
	322	6,307,040 B1	10-23-2001	Cook et al.	
	323	6,326,358 B1	12-04-2001	Manoharan	
	324	6,326,478	12-04-2001	Cheruvallath et al.	
	325	6,331,617 B1	12-18-2001	Weeks et al.	
	326	6,335,432 B1	01-01-2002	Segev	
	327	6,335,434 B1	01-01-2002	Guzaev et al.	
	328	6,335,437 B1	01-01-2002	Manoharan et al.	
	329	6,344,436 B1	02-05-2002	Smith et al.	
	330	6,358,931 B1	03-19-2002	Cook et al.	
	331	6,365,379 B1	04-02-2002	Lima et al.	
	332	6,395,437 B1	05-28-2002	Wollesen	
	333	6,395,492 B1	05-28-2002	Manoharan et al.	
	334	6,410,702 B1	06-25-2002	Swaminathan et al.	
	335	6,414,127	07-02-2002	Lin et al.	
	336	6,420,549 B1	07-16-2002	Cook et al.	
	337	6,426,220	07-30-2002	Bennett et al.	
	338	6,436,640 B1	08-20-2002	Simmons et al.	

Examiner	Date	
Signature	Considered	

	Substitute for 1449/PTO			Complete if Known		
Substitute for 1	1449/P1O			Application Number	10/701,007	
INFORMATION DISCLOSURE				Filing Date	November 4, 2003	
STA	LEMENT E	BY APPLIC	CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet	14	of	56	Attorney Docket Number	ISIS-5325	

	U. S. PATENT DOCUMENTS								
Examiner Initials	Cite No.	Document Number Number – Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear				
	339	6,440,943 B1	08-27-2002	Cook et al.					
	340	6,444,806 B1	09-03-2002	Veerapanani et al.					
	341	6,465,628	10-15-2002	Ravikumar et al.					
	342	6,476,205 B1	11-05-2002	Buhr et al.					
	343	6,486,308 B2	11-26-2002	Kutyavin et al.					
	344	6,506,559 B1	01-14-2003	Fire et al.					
	345	6,525,031 B2	02-25-2003	Manoharan					
	346	6,528,631 B1	03-04-2003	Cook et al.					
	347	6,531,584 B1	03-11-2003	Cook et al.					
	348	6,534,639 B1	03-18-2003	Manoharan et al.					
	349	6,559,279 B1	05-06-2003	Manoharan et al.					
	350	6,573,072 B1	06-03-2003	Goodchild					
	351	6,593,466	07-15-2003	Manoharan et al.					
	352	6,656,730	12-02-2003	Manoharan					
	353	6,670,461	12-30-2003	Wengel et al.					
	354	6,673,611 B2	01-06-2004	Thompson et al.					
	355	6,683,167 B2	01-27-2004	Metelev et al.					
	356	6,794,499	09-21-2004	Wengel et al.					
	357	6,818,759 B2	11-16-2004	Beigelman et al.					
	358	6,849,726 B2	02-01-2005	Usman et al.					
	359	6,887,906	05-03-2005	Teng et al.					
	360	7,022,828 B2	04-04-2006	McSwiggen					
	361	RE34,069	09-15-1992	Koster et al.					

Examiner	Date	
Signature	Considered	

	Substitute for 1449/PTO			Compl	ete if Known
Substitute for 7				Application Number	10/701,007
INFORMATION DISCLOSURE				Filing Date	November 4, 2003
STA	STATEMENT BY APPLICANT			First Named Inventor	Charles Allerson
				Art Unit	1635
(use as many sheets as necessary)				Examiner Name	Jane J. Zara
Sheet	15	of	56	Attorney Docket Number	ISIS-5325

Examiner	Cite No	Foreign Patent Document	Publication Date	Name of Patentee or	Pages, Columns,	Ιт
Initials	One No	Country Code- Number -Kind Code (if known)	MM-DD-YYYY	Applicant of Cited Document	Lines, Where Relevant Passages or Relevant Figures Appear	
	362	CA 2,017,369 C	01-23-2001	Roche Diagnostics GmbH		
	363	DE 10100588 A1	07-18-2002	Ribopharma		Х
	364	DE 3915432 A1	11-15-1990	Klockner-Humboldt-Deutz AG		Х
	365	DE 4110085 A1	01-10-1992	Boehringer Ingelheim Int'l. GmbH		Х
	366	EP 0260032 A2	03-16-1988	Ajinmoto Co., Inc.		
	367	EP 0266168 A2	05-04-1988	Amoco Corp.		
	368	EP 0269574 A2	06-01-1988	Nippon Zoki Pharmaceutical Co. Ltd.		
	369	EP 0287313 A2	10-19-1988	Marquez		
	370	EP 0339330 A2	11-02-1989	Spradau, Hans F.W.		
	371	EP 0417999 A1	03-20-1991	The Wellcome Foundation Limited		
	372	EP 1389637 A1	02-18-2004	Atugen AG		
	373	EP 339842 A2	11-02-1989	Ajinomoto KK		
	374	JP 2-264792 A	10-29-1990	Ajinomoto KK		
	375	WO 00/76554 A1	12-21-2000	Isis Pharmaceuticals, Inc.		
	376	WO 01/049687 A2	07-12-2001	K.U. Leuven Research & Development		
	377	WO 01/48183 A2	07-05-2001	Devgen NV		
	378	WO 02/36743 A2	05-10-2002	Isis Pharmaceuticals, Inc.		
	379	WO 02/38578 A1	05-16-2002	Chattopadhyaya		
	380	WO 03/004602 A2	01-16-2003	Isis Pharmaceuticals, Inc.		
	381	WO 03/070918 A2	08-28-2003	Ribozyme Pharm Inc.		
	382	WO 2004/015107 A2	02-19-2004	Atugen AG		
	383	WO 2004/041889 A2	05-21-2004	Isis Pharm.		

Signature

Considered

	Substitute for 1449/PTO			Complete if Known		
Substitute for 1	1449/P1O			Application Number	10/701,007	
INFORMATION DISCLOSURE				Filing Date	November 4, 2003	
STA	LEMENT E	BY APPLIC	CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet	16	of	56	Attorney Docket Number	ISIS-5325	

				OCUMENTS	
Examiner Initials	Cite No	Foreign Patent Document Country Code- Number -Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	384	WO 2004/043977 A2	05-27-2004	Isis Pharm.	
	385	WO 2004/043978 A2	05-27-2004	Isis Pharm.	
	386	WO 2004/043979 A2	05-27-2004	Isis Pharm.	
	387	WO 2004/044133 A2	05-27-2004	Isis Pharm.	
	388	WO 2004/044136 A2	05-27-2004	Isis Pharm.	
	389	WO 2004/044138 A2	05-27-2004	Isis Pharm.	
	390	WO 2004/044139 A2	05-27-2004	Isis Pharmaceuticals Inc.	
	391	WO 2004/044140 A2	05-27-2004	Isis Pharm.	
	392	WO 2004/083430 A2	09-30-2004	Elmen et al.	
	393	WO 2004/097049 A1	11-11-2004	Isis Pharmaceuticals, Inc.	
	394	WO 2004/113496 A2	12-29-2004	Isis Pharm.	
	395	WO 2005/027962 A2	03-31-2005	Isis Pharm.	
	396	WO 90/15814 A1	12-27-1990	Meiogenics, Inc.	
	397	WO 91/06556 A1	05-16-1991	Gilead Sciences, Inc.	
	398	WO 91/10671 A1	07-25-1991	Isis Pharmaceuticals, Inc.	
	399	WO 91/15499 A1	10-17-1991	Europaisches Laboratorium Fur Molekularbiologie	
	400	WO 92/02258 A1	02-20-1992	Isis Pharmaceuticals, Inc.	
	401	WO 92/03452 A1	03-05-1992	Isis Pharmaceuticals, Inc.	
	402	WO 92/03568 A1	03-05-1992	Isis Pharmaceuticals, Inc.	
	403	WO 92/07065 A1	04-30-1992	Max Planck Gesellschaft	
	404	WO 92/20822 A1	11-26-1992	Isis Pharmaceuticals, Inc.	
	405	WO 92/20823 A1	11-26-1992	Isis Pharmaceuticals, Inc.	
	406	WO 92/22651 A1	12-23-1992	Isis Pharmaceuticals, Inc.	

Substitute for 1449/PTO				Complete if Known		
				Application Number	10/701,007	
	RMATION			Filing Date	November 4, 2003	
STATEMENT BY APPLICANT				First Named Inventor	Charles Allerson	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Jane J. Zara	
Sheet	17	of	56	Attorney Docket Number	ISIS-5325	

	FOREIGN PATENT DOCUMENTS								
Examiner Initials	Cite No	Foreign Patent Document Country Code- Number -Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	Т			
	407	WO 93/07883 A1	04-29-1993	Isis Pharmaceuticals, Inc.					
	408	WO 93/24510 A1	12-09-1993	Centre National de la Recherche					
	409	WO 94/02498 A1	02-03-1994	Worcester Foundation for Expermimental Biology					
	410	WO 94/02499 A1	02-03-1994	Hybridon, Inc.					
	411	WO 94/02501 A1	02-03-1994	Isis Pharmaceuticals, Inc.					
	412	WO 94/17093 A1	08-04-1994	Hybridon, Inc.					
	413	WO 94/26764 A1	11-24-1994	Centre National de la Recherche					
	414	WO 96/07392 A2	03-14-1996	Hybridon, Inc.					
	415	WO 96/11205 A1	04-18-1996	Isis Pharmaceuticals, Inc.					
	416	WO 97/26270 A2	07-24-1997	Ribozyme Pharm.					
	417	WO 97/30064 A1	08-21-1997	Stichting REGA					
	418	WO 97/46570 A1	12-11-1997	Isis Pharmaceuticals, Inc.					
	419	WO 98/16550 A1	04-23-1998	Isis Innovation Limited					
	420	WO 98/39352 A1	09-11-1998	Imanishi					
	421	WO 98/52614 A2	11-26-1998	The Board of Trustees of the Leland Stanford Junior Univ.					

Examiner	D	<b>Date</b>	
Signature	C	Considered	

	1440/PT0			Complete if Known		
Substitute for 1	1449/PTO			Application Number	10/701,007	
	RMATION			Filing Date	November 4, 2003	
STATEMENT BY APPLICANT			CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet	18	of	56	Attorney Docket Number	ISIS-5325	

		NON PATENT LITERATURE DOCUMENTS	
Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), Volume-issue Number(s), publisher, city and/or country where published.	Т
	422	Abe, A., et al., "Conformational energies and the random-coil dimensions and dipole moments of the polyoxides CH3O[CH2)yO]xCH3," J. Am. Chem. Soc., 1976, 98(21), 6468-6476	
	423	Afonina, I. et al., "Sequence-specific arrest of primer extension on single-stranded DNA by an oligonucleotide-minor groove binder conjugate," Proc. Natl. Acad. Sci. USA (1996) 93:3199-3204.	
	424	Agrawal, et al., "Oligodeoxynucleoside Phosphoramidates and Phosphorothioates as Inhibitors of Human Immunodeficiency Virus" Proc. Natl. Acad. Sci. USA, 1988, 85, 7079-7083	
	425	Agarwal, et al., "Synthesis and Enzymatic Properties of Deoxyribooligonucleotides Containing Methyl and Phenylphosphonate Linkages", Nucleic Acid Research 1979, 6, 3009-3024	
	426	Agrawal, S. et al., "Synthesis and Anti-HIV Activity of Oligoribonucleotides and Their Phosphorothioate Analogs," Ann. N.Y. Acad. Sci., 1992, 2-10	
	427	Agrawal, S., "Antisense Oligonucleotides: Towards Clinical Trials," TIBTECH, 1996, 14, 376-388	
	428	Agris, et al., "Inhibition of Vesicular Stomatitis Virus Protein Synthesis and Infection by Sequence-Specific Oligodeoxyribonucleoside Methylphosphonates", Biochemistry 1986, 25, 6268-6275	
	429	Akashi, et al., "Novel Stationary Phases for Affinity Chromatography. Nucleobase-Selective Recognition of Nucleosides and Nucleotides on Poly(9-vinyladenine)-Supported Silica Gel)", Chem. Letters, 1988, 1093-1096	
	430	Alahari, "Novel chemically modified oligonucleotides provide potent inhibition of P-glycoprotein expression," J. Pharmacology and Experimental Therapeutics, 1998, 286(1), 419-428	
	431	Alberts, et al., "DNA-Cellulose Chromatography", Meth. Enzymol., 1971, 21, 198-217	
	432	Allerson, C.R. et al., Abstract of the 227th ACS National Meeting, Anaheim, CA, March 28-April 1, 2004	
	433	Allerson, C.R. et al., "Fully 2'-Modified Oligonucleotide Duplexes with Improved in Vitro Potency and Stability Compared to Unmodified Small Interfering RNA," J. Med. Chem., 2005, 48, 901-904	
	434	Altschul, S.F. et al., "Basic Local Alignment Search Tool," J. Mol. Biol., 1990, 215, 403-410	

Examiner	Date	
Signature	Considered	

Substitute for 1449/PTO				Complete if Known		
Substitute for 1	1449/P1O			Application Number	10/701,007	
	RMATION			Filing Date	November 4, 2003	
STATEMENT BY APPLICANT			ANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet	19	of	56	Attorney Docket Number	ISIS-5325	

	NON PATENT LITERATURE DOCUMENTS	
435	Ambros, V. et al., "A uniform system for MicroRNA annotation," RNA (2003) 9: 277-279	
436	Ambros, V. et al., "MicroRNAs and Other Tiny Endogenous RNAs in C. elegans, "Curr Biol. (2003) 13: 807-818	
437	Ambros, V. et al., "MicroRNAs: Tiny Regulators with Great Potential," Cell (2001) 107: 823-826	
438	Antopolsky, M. et al., "Peptide-Oligonucleotide Phosphorothioate Conjugates with Membrane Translocation and Nuclear Localization Properties," Bioconjuxate Chem. (1999) 10(4):598-606.	
439	Arar, K. et al., "Synthesis and Antiviral Activity of Peptide-Oligonucleotide Conjugates Prepared by Using Na-(Bromoaceytl)peptides," Bioconjugate Chem. (1995) 6(5):573-577.	
440	Arndt-Jovin, et al., "Covalent Attachment of DNA to Agarose", Eur. J. Biochem., 1975, 54, 411-418	
441	Arnott, S., et al., "Optimised parameters for A-DNA and B-DNA," Biochem. & Biophys. Res. Comm., 1972, 47(6), 1504-1510	
442	Arya, S. K. et al., "Alnhibition of RNA Directed DNA Polymerase of Murine Leukemia Virus by 2'-O-Alkylated Polyadenylic Acids," Biochemical and Biophysical Research Communications, 1974, 59(2), 608-615	
443	Arya, S. K. et al., "Inhibition of Synthesis of Murine Leukemia Virus in Cultured Cells by Polyribonucleotides and Their 2'-O-Alkyl Derivatives," Molecular Pharmacology, 1976, 12, 234-241	
444	Asseline, U. et al., "Nucleic acid-binding molecules with high affinity and base sequence specificity: Intercalating agents covalently linked to oligodeoxynucleotides," Proc. Natl. Acad. Sci USA (1984) 81: 3297-3301	
445	Astriab-Fisher et al., "Conjugates of antisense olgonucleotides with the TAT and antennapedia cell-penetrating peptides: effects on cellular update, binding to target sequences and biologic actions," Pharmaceutical Research (2002) 19(6): 744-754	
446	Astriab-Fisher, A. et al., "Antisense Inhibition of P-glycoprotein Expression Using Peptide-Oligonucleotide Conjugates," Biochem. Pharmacol. (2000) 60, 243-90.	
447	Baker, B. F. et al., "Oligonucleotide-europium complex conjugate designed to cleave the 5' cap structure of the ICAM-I transcript potentiates antisense activity in cells," Nucleic Acids Res. (1999) 27(6):1547-1551.	
448	Bartel, B. et al., "MicroRNAs: At the Root of Plant Development," Plant Physiol. (2003) 132: 709-717	

Examiner

Date

0.1.11.1.6.4440/PTO				Complete if Known		
Substitute for 1449/PTO				Application Number	10/701,007	
		I DISCLOS		Filing Date	November 4, 2003	
STATEMENT BY APPLICANT			CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet	20	of	56	Attorney Docket Number	ISIS-5325	

	NON PATENT LITERATURE DOCUMENTS
449	Bayer, E. et al., "A New Support for Polypeptide Synthesis in Columns," Tetrahedron Letters, 1970, 51, 4503-4505
450	Beaucage et al. "The Functionalization of Oligonucleotides Via Phosphoramidite Derivatives", (1993) Tetrahedron 49(10):1925-1963
451	Beaucage S. and Iyer, R., "Advances in the synthesis of oligonucleotides by the phosphoramidite approach", Tetrahedron Letters, 1992, 48, 2223-2311
452	Beaucage S. and Iyer, R., "The synthesis of modified oligonucleotides by the phosphoramidite approach and their applications", Tetrahedron, 1993, 49, 6123-6194
453	Beaucage, S.L. et al., "Deoxynucleoside Phosphoramidites-A New Class of Key Intermediates for Deoxypolynucleotide Synthesis,", Tetrahedron Letts., 1981, 22, 1859-1862
454	Berger, "Crystal structures of B-DNA with incorporated 2'-deoxy-2'-fluoro-arabino-furanosyl thymines: implications of conformational preorganization for duplex stability," Nucleic Acids Research, 1998, 26, 2473-2480
455	Bevilacqua et al., "Minor-Groove Recognition of Double-Stranded RNA by the Double-Stranded RNA-Binding Domain from the RNA-Activated Protein Kinase PKR," Biochemistry, 1996, 35, 9983-9994
456	Bhat, et al., "A Simple and Convenient Method for the Selective N-Acylations of Cytosine Nucleosides", Nucleosides and Nucleotides, 1989, 8, 179-183
457	Biggadike, et al., "Short convergent route to homochiral carbocylic 2'-deoxynucleosides and carbocyclic robonucleosides", J. Chem. Soc. Chem. Commun. 1987, 1083-1084
458	Blanks, et al., "An oligodeoxynucleotide affinity column for the isolation of sequence specific DNA binding proteins", Nucleic Acids Res., 1988, 16, 10283-10299
459	Blomberg, P., "Control of replication of plasmid R1: the duplex between the antisense RNA, CopA, and its target, CopT, is processed specifically in vivo and in vitro by Rnase III", EMBO J., 1990, 9, 2331-2340
460	Bollig, F. et a]., "Affinity purification of ARE-binding proteins identifies poly(A)-binding protein 1 as a potential substrate in MK2-induced mRNA stabilization," Biochem. Bioophys. Res. Commun. (2003) 301: 665-670
461	Bongartz, JP. et al., "Improved biological activity of antisense oligonucleotides conjugated to a fusogenic peptide," Nucleic Acids Res. (1994) 22(22):4681-4688.
462	Bonora, G. M. et al., "Antisense activity of an anti-HIV oligonucleotide conjugated to linear and branched high molecular weight polyethylene glycols," Farmaco (1998) 53:634-637.

Examiner	Date	
Signature	Considered	

Collections for AAAO/PTO				Complete if Known		
Substitute for 1	1449/PTO			Application Number	10/701,007	
		I DISCLOS		Filing Date	November 4, 2003	
STATEMENT BY APPLICANT			CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet	21	of	56	Attorney Docket Number	ISIS-5325	

	NON PATENT LITERATURE DOCUMENTS	
463	Bonora, G. M. et al., "Biological Properties of Antisense Oligonucleotides Conjugated to - Different High-Molecular Mass Poly(Ethy1en Glycols)," Nucleosides Nucleotides (1999) 18(6&7):1723-1725	
464	Bonora, G.M., et al., "A liquid-phase process suitable for large-scale synthesis of phosphorothioate oligonucleotides," Organic Process Res. & Develop., 2000, 225-231	
465	Borer, et al., "Stability of ribonucleic acid double-stranded helices," J. Mol. Biol., 1974, 86, 843-853	
466	Braasch et al., "Antisense inhibition of gene expression in cells by oligonucleotides incorporating locked nucleic acids: effect of mRNA target sequence and chimera design," Nucleic Acids Research, 2002, 30, 5160-5167	
467	Braasch, D.A. et al., "Locked nucleic acid (LNA): fine-tuning the recognition of DNA and RNA," Chem Biol, 2001, 8, 1-7	
468	Braasch, D.A., et al., "Novel antisense and peptide nucleic acid strategies for controlling gene expression," Biochemistry, April 9, 2002, 41(14), 4503-4510	
469	Branda et al., "Amplification of antibody production by phosphorothioate oligodeoxynucleotides," J. Lab. Clin. Med., 1996, 128(3), 329-338	
470	Branden, L. J. et al., "A peptide nucleic acid-nuclear localization signal fusion that mediates nuclear transport of DNA," Nature Biotech (1999) 17:784-787.	
471	Brazma, A., et al., "Gene expression data analysis," FEBS Lett., 2000, 480, 17-24	
472	Brill, et al., "Synthesis of Oligodeoxynucleoside Phosphorodithioates Via Thioamidites", J. Am. Chem. Soc. 1989, 111, 2321-2322	
473	Brown-Driver et al., "Inhibition of Translation of Hepatitis C Virus RNA by 2'-Modified Antisense Oligonucleotides," Antisense Nucleic Acid Drug Dev. (1999) 9(2): 145-154	
474	Buhr, C.A. et al., "Oligodeoxynucleotides containing C-7 propyne analogs of 7-deaza-2'-deoxyguanosine and 7-deaza-2'-deoxyadenosine," Nucleic Acids Research, 1996, 24(15), 2974-2980	
475	Bunemann, et al., Immobilization of denatured DNA to macroporous supports: I. Efficiency of different coupling procedures", Nucleic Acids Res., 1982, 10, 7163-7180	
476	Bunemann, H., "Immobilization of denatured DNA to macroporous supports: II. Steric and kinetic parameters of heterogeneous hybridization reactions", Nucleic Acids Res., 1982, 10, 7181-7196	

Examiner	Date	
Signature	Considered	

0 L ("L L C 4440/DT0				Complete if Known		
Substitute for 1	1449/P1O			Application Number	10/701,007	
		DISCLOS		Filing Date	November 4, 2003	
STATEMENT BY APPLICANT				First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet	22	of	56	Attorney Docket Number	ISIS-5325	

	NON PATENT LITERATURE DOCUMENTS	
477	Butke, et al., "Facile synthesis of 2'amino-2deoxynucleoside from the corresponding arabino derivative," Nucleic Acid Chemistry, 1986, Part Three, 149-152	
478	Butler, M. et al., "Specific Inhibition of PTEN Expression Reverses Hyperglycemia in Diabetic Mice," Diabetes, 2002, 51, 1028-1034	
479	Caplen et al., "dsRNA-mediated gene silencing in cultured Drosophila cells: a tissue culture model for the analysis of RNA interference," GENE (2000) 252: 95-105	
480	Carmell, M.A. et al., "the argonaute family: tentacles that reach into RNAi, developmental control, stem cell maintenance, and tumorigenesis," Genes and Development, 2002, 16, 2733-2742	
481	Carulli, J.P., et al., "High throughput analysis of differential gene expression," J. Cellular Biochem. Suppl., 1998, 30(31), 286-296	
482	Caruthers, M., "Synthesis of Oligonucleotides and Oligonucleotide Analogues", in "Oligonucleotides. Antisense Inhibitors of Gene Expression.", J.S. Cohen, Ed., CRC Press, Inc., 7-24, (1989)	
483	Castle, et al., "Imidazo[4, 5-D]pyridazines. I. Synthesis of 4,7-disubstituted derivatives", Journal of Organic Chemistry, 1958, 23, 1534-1538	
484	Cazalla, D. et al., "Nuclear Export and Retention Signals in the RS Domain of SR Proteins," Mol. Cell. Biol. (2002) 22(19):6871-6882.	
485	Cazenave, C. et al., "Enzymatic amplification of translation inhibition of rabbit β-globin mRNA mediated by anti-messenger oligodeoxynucleotides covalently linked to intercalating agents", Nucl. Acids Res., 1987, 15, 4717-4736	
486	Celis, J.E., et al., "Gene expression profiling: monitoring transcription and translation production using DNA microarrays and proteomics," FEBS Lett., 2000, 480, 2-16	
487	Cerutti, H., "RNA interference: traveling in the cell and gaining functions?" Trends in Genetics (2003) 19(1): 39-46	
488	Chaloin, L. et al., "Design of Carrier Peptide-Oligonucleotide Conjugates with Rapid Membrane Translocation and Nuclear Localization Properties," Biochem. Biophys. Res. Commun. (1998) 243:601-608	
489	Chaput, J.C., et al., "DNA polymerase-mediated DNA synthesis on a TNA template," J. Am. Chem. Soc., 2003, 125, 856-857	

Examiner	Date	
Signature	Considered	

0 L ("L L C 4440/DT0				Complete if Known		
Substitute for 1	1449/P1O			Application Number	10/701,007	
		DISCLOS		Filing Date	November 4, 2003	
STATEMENT BY APPLICANT				First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet	23	of	56	Attorney Docket Number	ISIS-5325	

	NON PATENT LITERATURE DOCUMENTS	
490	Chen and Wu, "Studies on Fluoroalkylation and Fluroalkoxylation. Part 33. Direct Trifluoromethylation of Aryl Halides with Fluorosulphonyldifluoromethyl lodide in the Presence of Copper: an Electron Transfer Induced Process," J. Chem. Soc., Perkin Transactions, 1989, 1, 2385-2387.	
491	Chiang et al., "Antisense Oligonucleotides Inhibit Intercellular Adhesion Molecule 1 Expression by Two Distinct Mechanisms," J. Biol. Chem., 1991, 266, 18162-18171	
492	Chiu, YL. et al., "RNAi in human cells: basic structural and functional features of small interfering RNA," Molecular Cell, September 2002, 10, 549-561	
493	Chladek, et al., "Facile Synthesis of 2'Amino-2'Deoxyadenosine," J. Carbohydtrates, Necleosides & Nucleotides, 1980, 7, 63-75.	
494	Chodosh, et al., "A Single Polypeptide Possesses the Binding and Transcription Activities of the Adenovirus Major Late Transcription Factor", Mol. Cell. Biol., 1986, 6, 4723-4733	
495	Choung, S. et al., "Chemical modification of siRNAs to improve serum stability without loss of efficacy," Biochemical and Biophysical Research Communications, 2006, 342, 919-927	
496	Christofferson et al., "Ribozymes as human therapeutic agents", J. Med. Chem., 1995, 38(12), 2023-2037	
497	Chun-Nam Lok et al., "Potent gene-specific inhibitory properties of mixed backbone antisense oligonucleotides comprised of 2' -deoxy-2' -fluoro-D-arabinose and 2' -deoxyribose nucleotides," Biochemistry, 2002, 41, 3457-3467	
498	Cogoni, C. et al., "Post-transcriptional gene silencing across kingdoms," Curr. Opin. Genet Dev., 2000, 10(6), 638-643	
499	Cohen, G. L. et al., "Sequence Dependent Binding of cis-Dichlorodiamrnineplatinum(II) to DNA," J. Am. Chem. Soc. (1980) 102(7), 2487-2488.	
500	Concise Encyclopedia of Polymer Science and Engineering, pgs. 858-859, Kroschwitz, J.I., Ed., John Wiley & Sons, 1990	
501	Constant et al., "Heterodimeric Molecules Including Nucleic Acid Bases and 9-Aminoacridine Spectroscopic Studies, Conformations, and Interactions with DNA", Biochemistry, 1988, 27, 3997-4003	
502	Conte, M.R., et al., "Conformational properties and thermodynamics of the RNA duplex r(CGCAAAUUUGCG)2: comparison with the DNA analogue d(CGCAAATTTGCG)2," Nucleic Acids Res., 1997, 25(13), 2627-2634	
503	Cook, "Medicinal chemistry of antisense oligonucleotides - future opportunities," Anti-Cancer Drug Design, 1991, 6, 585-607	

Examiner	Date	
Signature	Considered	

0 L ("L L C 4440/DT0				Complete if Known		
Substitute for 1	1449/P1O			Application Number	10/701,007	
		DISCLOS		Filing Date	November 4, 2003	
STATEMENT BY APPLICANT				First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet	24	of	56	Attorney Docket Number	ISIS-5325	

		NON PATENT LITERATURE DOCUMENTS				
	504	Copy of PCT International Search Report dated January 24, 2005 (PCTUS03/35087)				
	505 Copy of the PCT International Search Report dated August 23, 2004 (PCT/US03/35063)					
	506 Corey, D. R. et al., "Generation of a Hybrid Sequence-Specific Single-Stranded Deoxyribonuclease," Science (1987) 238:1401-1403.					
	507	Corey, D. R. et al., "Sequence-Selective Hydrolysis of Duplex DNA by an Oligonucleotide-Directed Nuclease," J. Am. Chem. Soc. (1989) 111(22):8523-8525.				
	508	Corey, D. R., "48000-fold Acceleration of Hybridization by Chemically Modified Oligonucleotides," J. Am. Chem. Soc. (1995) 117(36):9373-9374.				
	509	Cornell, W. D. et al., "A Second Generation Force Field for the Simulation of Proteins, Nucleic Acids, and Organic Molecules," J. Am. Chem. Soc., 1995, 117, 5179-5197				
	Cossum, P.A. et al., "Disposition of the 14C-Labeled Phosphorothioate Oligonucleotide ISIS 2105 after Intravenous Administration to Rats," J. Pharmacol. Exp. Ther., 1993, 267(3), 1181-1190					
	511	Couzin, J., "Small TNAs Make Big Splash," Science (2002) 298: 2296-2297				
	512 Crawford, J.M., "Role of Vesicle-Mediated Transport Pathways in Hepatocellular Bile Secretion," Semin. Liver Dis., 1996, 16(2), 169-189					
	Crooke, et al., "Kinetic characteristics of Escherichia coli Rnase H1: cleavage of various antisense oligonucleotide-RNA duplexes", Biochem. J., 1995, 312, 599-608					
	514	Crooke, et al., "Pharmacokinetic Properties of Several Novel Oligonucleotide Analogs in mice", J. Pharmacol. Exp. Therm., 1996, 277, 923-927				
	515	Crooke, S.T. and Bennett, C.F., "Progress in Antisense Oligonucleotide Therapeutics", Annu. Rev. Pharmacol. Toxicol., 1996, 36, 107-129				
	516	Crooke, S.T., Antisense Research & Application, Chapter 1, Pages 1-50, Publ. Springer-Verlag, Ed. S.T. Crooke (1998).				
	Cummins, L.L. et al., "Characterization of fully 2'modified oligoribonucleotide hetero- and homoduplex hybridization and nuclease sensitivity," Nucleic Acids Research, 1995, 23(11), 2019-2024					
	518	Dagle, et al., "Pathways of Degradation and Mechanism of Action of Antisense Oligonucleotides in Xenopus laevis Embryos", Antisense Res. And Dev., 1991, 1, 11-20				
	519	Dagle, et al., "Physical properties of oligonucleotides containing phosphoramidate-modified internucleoside linkages", Nucleic Acids Research, 1991, 19, 1805-1810				
Examiner Signature		Date Considered				

0 L 51 L 5 4440/DT0				Complete if Known		
Substitute for 1	1449/P1O			Application Number	10/701,007	
		DISCLOS		Filing Date	November 4, 2003	
STA	LEMENT E	BY APPLIC	CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet	25	of	56	Attorney Docket Number	ISIS-5325	

	NON PATENT LITERATURE DOCUMENTS
520	Dagle, et al., "Targeted degradation of mRNA in Xenopus oocytes and embryos directed by modified oligonucleotides: studies of An2 and cyclin in embryogenesis", Nucleic Acids Research, 1990, 18, 4751-4757
521	Dahl, B.H. et al., "A Highly Reactive, Odourless Substitute for Thiphenol/Triethylmaine as a Deprotection Reagent in the Synthesis of Oligonucleotides and their Analogues," Acta Chem. Scand., 1990, 44, 639-641
522	Dake, et al., "Purification and Properties of the Major Nuclease from Mitochondria of Saccharomyces cerevisiae", J. Biol. Chem., 1988, 263, 7691-7702
523	Damha, et al., "Solution and solid phase chemical synthesis of arabinonucleotides", Can J. Chem., 1989, 831-839
524	Damha, M.J., et al., "Hybrids of RNA and arabinonucleic acids (ANA and 2'F-ANA) are substrates of ribonuclease H," J. Am. Chem. Soc., 1998, 120, 12976-12977
525	Dande, P. et al., Abstract from The 227th ACS National Meeting, Anaheim, CA, March 28-April 1, 2004
526	Day, et al., "Immobilization of polynucleotides on magnetic particles", Biochem. J., 1991, 278, 735-740
527	De las Heras, et al., "3'-C-Cyano-3'-Deoxythymidine," Tetrahedron Letters, 1988, 29, 941-944
528	De Mesmeker, et al., "Antisense Oligonucleotides", Acc. Chem. Res., 1995, 28, 366-374
529	DeClercq, E. et al., "Influence of various 2- and 2'-substituted polyadenyl acids on murine leukemia virus reverse transcriptase," Cancer Letters, 1979, 7, 27-37
530	Dellinger, D.J. et al., "Solid-Phase Chemical Synthesis of Phosphonoacetate and Thiophosphonoacetate Oligodexynucleotides," J. Am. Chem. Soc., 2003, 125(4), 940-950
531	Denny, W.A., "DNA-intercalating ligands as anti-cancer drugs: prospects for future design," Anti-Cancer Drug Design, 1989, 4, 241-263
532	Dignam, et al., "Accurate transcription initiation by RNA polymerase II in a soluble extract from isolated mammalian nuclei," Nucleic Acids Res., 1983, 11, 1475-1489
533	Divakar, et al., "Approaches to the Synthesis of 2'-Thio Analogues of Pyrimidine Ribosides", J. Chem. Soc., Perkins Trans., I, 1990, 969-974
534	Divakar, et al., "Reaction Between 2,2'-Anhydro-1-β-D-arrabinofuranosyluracil and Thiolate Ions", J. Chem. Soc., Perkins Trans. I, 1982, 1625-1628

Examiner	Date	
Signature	Considered	

0 L ("L L C 4440/DT0				Complete if Known		
Substitute for 1	1449/P1O			Application Number	10/701,007	
	RMATION			Filing Date	November 4, 2003	
STATEMENT BY APPLICANT				First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet	26	of	56	Attorney Docket Number	ISIS-5325	

	NON PATENT LITERATURE DOCUMENTS						
535	Dreyer, et al., "Sequence-specific cleavage of single-stranded DNA: Oligodeoxynucleotide-EDTA-Fe(II)", Proc. Natl. Acad. Sci. USA, 1985, 82, 968-972						
536	Drmanac, et al., "DNA Sequence Determination by Hybridization: A Strategy for Efficient Large-Scale Sequencing", Science, 1993, 260, 1649-1652						
537	Duff, R. J. et al., "[17] Intrabody Tissue-Specific Delivery of Antisense Conjugates in Animals: Ligand-Linker-Antisense Oligomer Conjugates," Methods Enzymol. (2000) 313:297-321.						
538	Duncan, et al., "Affinity Chromatography of a Sequence-Specific DNA Binding Protein Using Teflon-Linked Oligonucleotides", Anal. Biochem., 1988, 169, 104-108						
539	Dunn, J.J. and Studier, F.W., "Effect of RNAase III Cleavage on Translation of Bacteriophage T7 Messenger RNAs", J. Mol. Biol., 1975, 99, 487-499						
540	Eckstein, et al., "Polynucleotides Containing 2'Chloro-2'Deoxyribose", Biochemistry, 1972, 11, 4336-4344						
541	Eddy, S.R., "Non-Coding RNA Genes and the Modern RNA World," Nature Rev. Genetics (2001) 2: 919-929						
542	Eder, P.S. and Walder, J.A., "Ribonuclease H from K562 Human Erythroleukemia Cells", J. Biol. Chem., 1991, 266, 6472-6479						
543	Efimov, V. A. et al., "Synthesis of Polyethylene Glycol - Oligonucleotide Conjugates," Bioorg. Khim. (1993) 19(8):800-804.						
544	Egli, M. et al., "RNA Hydration: A Detailed Look," Biochemistry, 1996, 35, 8489-8494						
545	Elayadi, A.N. et al., "Application of PNA and LNA oligomers to chemotherapy," Curr. Opin. Investig. Drugs, 2001, 2(4), 558-561						
546	Elela, et al., "RNase III Cleaves Eukaryotic Preribosomal RNA at a U3 snoRNP-Dependent Site", Cell, 1996, 85, 115-124						
547	Elmén, J. et al., "Locked nucleic acid (LNA) mediated improvements in siRNA stability and functionality," Nucleic Acids Res. 2005, 33(1), 439-447						
548	Englisch, U. And Gauss, D.H., "Chemically Modified Oligonucleotides as Probes and Inhibitors", Angewandt Chemie, International Edition Engl., 1991, 30, 613-629						
549	EP Supplementary Search Report for EP 03716922 dated May 12, 2006						
550	Fahy, et al., "Design and synthesis of polyacrylamide-based oligonucleotide supports for use in nucleic acid diagnostics", Nucl. Acids Res., 1993, 21, 1819-1826						

Examiner	Date	
Signature	Considered	

Substitute for 1449/PTO				Complete if Known		
				Application Number	10/701,007	
INFORMATION DISCLOSURE				Filing Date	November 4, 2003	
STA	STATEMENT BY APPLICANT			First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet	27	of	56	Attorney Docket Number	ISIS-5325	

	NON PATENT LITERATURE DOCUMENTS							
551	Faria, M. et al., "Phosphoramidate oligonucleotides as potent antisense molecules in cells and in vivo," Nature Biotech., 2001, 19, 40-44							
552	Fazakerley, G.V., et al., "A→Z transition in the synthetic hexanucleotide (dCdGfl)3," FEBS, 1985, 182(2), 365-369							
553	Fedoroff, O.Y. et al., "Structure of a DNA:RNA Hybrid Duplex," J. Mol. Biol., 1993, 233, 509-523							
554	Fire et al., "RNA-triggered gene silencing," TIG (1999) 15(9): 358-363							
555	Fire, A. et al., "Potent and specific genetic interference by double-stranded RNA in Caenorhabditis elegans," Nature, 1998, 391(6669), 806-811							
556	Firestone, R. A., "Low-Density Lipoprotein as a Vehicle for Targeting Antitumor Compounds to Cancer Cells," Bioconjugate Chern. (1994) 105-113.							
557	Fishel, et al., "Z-DNA Affinity Chromatography", Methods Enzymol., 1990, 184, 328-342							
558	Flanagan, W. M. et al., "A cytosine analog that confers enhanced potency to antisense oligonucleotides," Proc. Natl. Acad. Sci. USA, Mar. 1999, 96, 3513-3518							
559	Flanagan, W.M. et al., "Cellular penetration and antisense activity by a phenoxazine-substituted heptanucleotide," Nature Biotechnol. (1999) 17(1): 48-52							
560	Fluiter, K. et al., "In vivo tumor growth inhibition and biodistribution studies of locked nucleic acids (LNA) antisense oligonucleotides," Nucleic Acids Res., 2003, 31(3), 953-962							
561	Fodor, et al., "Light-Directed, Spatially Addressable Parallel Chemical Synthesis", Science, 1991, 251, 767-773							
562	Fox, et al., "Nucleosides. XVIII. Synthesis of 2'-Fluorothymidine, 2'-Flurodeoxyuridine, and Other 2'-Halogeno-2'-Deoxy Nucleosides 12", J Org. Chem., 1964, 29, 558-564							
563	Francis, A.W. et al., "Probing the Requirements for Recognition and Catalysis in Fpg and MutY with Nonpolar Adenine Isosteres," J. Am. Chem. Soc. (2003) 125(52): 16235-16242							
564	Fraser, A.G. et al., "Functional genomic analysis of C. elegans chromosome 1 by systemic RNA interference," Nature, 2000, 408, 325-330							
565	Freier, S. M. et al., "The ups and downs of nucleic acid duplex stability: structure–stability studies on chemically-modified DNA:RNA duplexes," Nucleic Acids Research, 1997, 25(22), 4429-4443							
566	Freskos, "Synthesis of 2'Deoxypyrimidine Nucleosides Via Copper (I) Iodine Catalysis," Nucleosides & Nucleotides, 1989, 8, 1075, 1076							

Examiner	Date	
Signature	Considered	

0 L 47 4 5 4449/PT0				Complete if Known		
Substitute for 1449/PTO				Application Number	10/701,007	
INFORMATION DISCLOSURE				Filing Date	November 4, 2003	
STA <sup>-</sup>	STATEMENT BY APPLICANT			First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet	28	of	56	Attorney Docket Number	ISIS-5325	

	NON PATENT LITERATURE DOCUMENTS						
567	Frieden, M. et al., 'Expanding the design horizon of antisense oligonucleotides with alpha-L-LNA," Nucleic Acids Res., 2003, 31(21), 6365-6372						
568	Fromageot, H.P.M. et al., "The Synthesis of Oligonucleotides," Tetrahedron, 1967, 23, 2315-2331						
569	Fuchs, B. et al., "Identification of Differentially Expressed Genes by Mutually Subtracted RNA Fingerprinting," Anal. Biochem., 2000, 286, 91-98						
570	Fusi, et al., "Ribonucleases from the extreme thermophilic archaebacterium S. Solfataricus", Eur. J. Biochem., 1993, 16, 305-310						
571	Gabrielsen, et al., AMagnetic DNA affinity purification of yeast transcription factor τ-a new purification principle for the ultrarapid isolation of near homogeneous factor", Nucleic Acids Research, 1989, 17, 6253-6267						
572	Gaffney, et al., "A New Strategy for the Protection of eoxyguanosine During Oligonucleotide Synthesis," Tetrahedron Letters, 1982, 23, 2257-2260						
573	Gait, M.J. et al., "Application of chemically synthesized RNA," RNA: Protein Interactions (1998) Smith (ed.), pp. 1-36						
574	Gait, M.J., "Oligoribonucleotides, Antisense Research and Applications, 1993, Crooke, S.T. and Lebleu, B. (eds.), CRC Press, Boca Raton, pp. 289-301						
575	Gallo, M. et al., "2'-C-Methyluridine phosphoramidite: a new building block for the preparation of RNA analogues carrying the 2'-hydroxyl group," Tetrahedron, 2001, 57(27), 5707-5713						
576	Gao, J. et al., "Expanded-Size Bases in Naturally Sized DNA: Evaluation of Steric Effects in Watson-Crick Pairing," J. Am. Chem. Soc. (2004) 126(38): 11826-11831						
577	Gbenle, "Simultaneous Isolation of Cytoplasmic Endoribonuclease and Exoribonucease of Trypanosoma Brucei", Mol. Biochem. Parasitol., 1985, 15, 37-47						
578	Gbenle, "Trypanosoma brucei: Calcium-Dependent Endoribonuclease is Associated with Inhibitor Protein", Exp. Parasitol., 1990, 71, 432-438						
579	Geary, R.S. et al., "Pharmacokinetic Properties of 2'-O-(2-Methoxyethyl)-Modified Oligonucleotide Analogs in Rats," J. Pharmacol. Exp. Therap., 1998, 296(3), 890-897						
580	Gerdes, K., et al., "Mechanism of Killer Gene Activation. Antisense RNA-dependent Rnase III Cleavage Ensures Rapid Turn-over of the Stable-Hok, SrnB and PndA Effector Messenger RNAs", J. Mol. Biol., 1992, 226, 637-649						
581	Gingeras, et al., "Hybridization properties of immobilized nucleic acids", Nucl. Acids Res., 1987, 15, 5373-5391						

Examiner	Date	
Signature	Considered	

0 L 11 L 5 4440/PT0				Complete if Known		
Substitute for 1449/PTO				Application Number	10/701,007	
		DISCLOS		Filing Date	November 4, 2003	
STATEMENT BY APPLICANT			CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Jane J. Zara	
Sheet	29	of	56	Attorney Docket Number	ISIS-5325	

	NON PATENT LITERATURE DOCUMENTS							
582	Going, J.J., et al., "Molecular pathology and future developments," Eur. J. Cancer, 1999, 35(14), 1895-1904							
583	Goldkorn, T. And Prockop, D.J., "A simple and efficient enzymatic method for covalent attachment of DNA to cellulose. Application for hybridization-restriction analysis and for in vitro synthesis of DNA probes", Nucleic Acids Res., 1986, 14, 9171-9191							
584	Gonzalez, C. et al., "Structure and Dynamics of a DNA-RNA Hybrid Duplex with a Chral Phosphorothioate Moiety: NMR and Molecular Dynamics with Conventional and Time-Averaged Restraints," Biochemistry, 1995, 34, 4969-4982							
585	Goodchild, et al., "Conjugates of Oligonucleotides and Modified Oligonucleotides: A Review of their Synthesis and Properties", Bioconjugate Chem., 1990, 1(3), 165-187							
586	Gorlach, M. et al., "The rnRNA Poly(A)-Binding Protein: Localization, Abundance, and RNABinding Specificity," Exp. Cells Res. (1994) 211:400-407							
587	Goss, T.A. and Bard, M., "High-performance affinity chromatography of DNA", J. Chromatogr., 1990, 508, 279-287							
588	Graham, et al., "Tritium Labeling of Antisense Oligonucleotides by Exchange with Tritiated Water," Nucleic Acids. Res., 1993, 16, 3737-3743							
589	Graham, M.J. et al., "In Vivo Distribution and Metabolism of a Phosphorothioate Oligonucleotide within Rat Liver after Intravenous Administration," J. Pharmacol. Exp. Therap., 1998, 286(1), 447-458							
590	Gravert, D.J., et al., "Organic synthesis on soluble polymer supports," Chem. Rev., 1997, 97, 489-509							
591	Griffey, R.H. et al., "2'-O-Aminopropyl Ribonucleotides: A Zwitterionic Modification that Enhances the Exonuclease Resistance and Biological Activity of Antisense Oligonucleotides," J. Med. Chem., 1996, 39(26), 5100-5109							
592	Griffin, B.E. et al., "The Synthesis of Oligoribonucleotides," Tetrahedron, 1967, 23, 2301-2313							
593	Grishok, A. et al., "Genetic Requirements for Inheritance of RNAi in C. elegans," Science, 2000, 287, 2494-2497							
594	Grünweller, A. et al., "Comparison of different antisense strategies in mammalian cells using locked nucleic acids, 2'-O-methyl RNA, phosphorothioates and small interfering RNA," Nucleic Acids Research, 2003, 31(12), 3185-3193							
595	Gryaznov, S. et al., "Oligodeoxynucleotide N3'P5' Phosphoramidates: Synthesis and Hybridization Properties," J. Am. Chem. Soc., 1994, 116(7), 3143-3144							

Examiner	Date	
Signature	Considered	

0 L (1) L ( AAAO/DTO				Complete if Known		
Substitute for 1449/PTO				Application Number	10/701,007	
		DISCLOS		Filing Date	November 4, 2003	
STATEMENT BY APPLICANT			CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Jane J. Zara	
Sheet	30	of	56	Attorney Docket Number	ISIS-5325	

		NON PATENT LITERATURE DOCUMENTS
	596	Guckian, K.M. et al., "Structure and Base Pairing Properties of a Replicable Nonpolar Isostere for Deoxyadenosine," J Org Chem (1998) 63(26);9652-9656
	597	Guillerm, D. et al., "Synthesis of 4'-fluoroadenosine as an inhibitor of S-adenosyl-L-homocysteine hydrolase," Bioorganic & Medicinal Chemistry Letters, 1995, 5(14), 1455-1460
	598	Guo, et al., "Direct fluorescence analysis of genetic polymorphisms by hybridization with oligonucleotide arrays on glass supports", Nucl. Acids Res., 1994, 22, 5456-5465
	599	Guo, S. et al., "par-1, a Gene Required for Establishing Polarity in C. elegans Embryos, Encodes a Putative Ser/Thr Kinase That is Asymmetrically Distributed," Cell, 1995, 81(4), 611-620
	600	Gura, T., "A silence that speaks volumes," Nature, 2000, 404, 804-808
	601	Guschlbauer, et al., "Nucleoside conformation is Determined by the Electronegativity of the Sugar Substituent," Nucleic Acids Res., 1980, 8, 1421-1433
	602	Guschlbauer, W. et al., "Poly-2'-deoxy-2'-fluoro-cytidylic acid: enzymatic synthesis, spectroscopic characterization and interaction with poly-inosinic acid," Nucleic Acid Research, 1977, 4(6),1933-1943
	603	Guschlbauer, W., et al., "Use of 2'-deoxy-2'-fluoro-necleosides in the study of polynucleotide conformation: a progress report," Nucleic Acid Research Symposium Series, 1982, 11,113-116
	604	Gutierrez, A.J. et al., "Antisense Gene Inhibition by C-5 Substituted Deoxyuridine-Containing Oligodeoxynucleotides," Biochemistry, 1997, 36(4), 743-748
	605	Guzaev, A. et al., "Conjugation of Oligonucleotides Via an Electrophilic Tether: N-Chloroacetarnidohexyl Phosphoramidite Reagent," Bioorg. Med. Chem. lett . (1998) 8:3671-3676.
	606	Haeuptle and Dobberstein, "Translation arrest by oligonucleotides complementary to mRNA coding sequences yields polypeptides of predetermined length", Nucleic Acids Res., 1986, 14, 1427-1448
	607	Hakimelahi, G.H. et al., "High Yield Selective 3'-Silylation of Ribonucleosides," Tetrahedron Lett., 1981, 22(52), 5243-5246
	608	Hall, J. et al., "Efficient sequence-specific cleavage of RNA using novel europium complexes conjugated to oligonucleotides," Chem. Biol. (1994) 1(3):185-190.
	609	Hamada et al., "Effects on RNA Interference in Gene Expression (RNAi) in Cultured Mammalian Cells of Mismatches and the Introduction of Chemical Modifications at the 3'Ends of siRNAs," Antisense and Nucleic Acid Drug Development (2002) 12:301-309
Examiner	T	Date

	0   1   1   1   1   1   1   1   1   1			Complete if Known		
Substitute for 1	1449/PTO			Application Number	10/701,007	
		I DISCLOS		Filing Date	November 4, 2003	
STA <sup>-</sup>	TEMENT E	BY APPLIC	CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet 31 of 56		56	Attorney Docket Number	ISIS-5325		

	NON PATENT LITERATURE DOCUMENTS
610	Hamilton et al., "A species of small antisense RNA in posttranscriptional gene silencing in plants," Science (1999) 286 (5441): 950-952
611	Hammond et al., "Post-Transcriptional Gene Silencing byDouble-Stranded RNA," Nature, 2001, 2, 110-119
612	Hansske, et al., "2'and 3'-ketonucleosides and their arabino and XYLO reduction products," Tetrahedron, 1984, 40, 125-135
613	Hariton-Gazal, E. et al., "Targeting of Nonkaryophilic Cell-Permeable Peptides into the Nuclei of Intact Cells by Covalently Attached Nuclear Localization Signals," Biochemistry (2002) 41(29):9208-9214.
614	Harry O'Kuru, R.E. et al., "A Short, Flexible Route toward 2'-C-Branched Ribonucleosides," J. Org. Chem., 1997, 62(6), 1754-1759
615	Heasman, J., "Morpholino Oligos: Making Sense of Antisense?" Dev. Biol., 2002, 243, 209-214
616	Henderson, B. R. et al., "A Comparison of the Activity, Sequence Specificity, and CRM1-Dependence of Different Nuclear Export Signals," Exp. Cell Res. (2000) 256:213-224.
617	Hertel, et al., "Synthesis of 2-deoxy-2,2-difluoro-D-ribose and 2-deoxy-2,2-difluoro-D-ribofuranosyl nucleosides," J. Org. Chem., 1988, 53, 2406-2409.
618	Hill, F. et al., "Polymerase recognition of synthetic oligodeoxyribonucleotides incorporating degenerate pyrimidine and purine bases," Proc. Natl. Acad. Sci. USA, 1998, 95, 4258-4263
619	Hobbs, J. et al., "Poly 2'-Deoxy-2'-Aminouridylic Acid," Biochem. Biophys. Res. Commun., 1972, 46(4), 1509-1515
620	Hobbs, J. et al., "Polynucleotides Containing 2'-Amino 2'-deoxyribose and 2'-Azido-2'-deoxyribose," Biochem., 1973, 12, 5138-5145
621	Hobbs, J. et al., "Polynucleotides Containing 2'-Chloro-2'-deoxyribose," Biochem., Eckstein et al., Ed., 1972, 11, 4336-4344
622	Hoffman, K., "Imidazole and its Derivatives" in The Chemistry of Heterocyclic Compounds, Weissberger, A., Ed.,Interscience Publishers, Inc., New York, 1953, 447
623	Hornbeck, P. et al., Enzyme-Linked Immunosorbet Assays (ELIASE)," Curr. Protocols Mol. Biol., 1991, John Wiley & Sons, pp. 11.2.1-11.2.22
624	Hornung, V. et al., "Sequence-specific potent induction of IFN-a by short ineterfering RNA in plasmacytoid dendritic cells through TLR7," Nature Med., 2005, 11(3), 263-270

Examiner	Date	
Signature	Considered	

	Out all the fact 4440/DTO			Complete if Known		
Substitute for 1449/PTO				Application Number	10/701,007	
		DISCLOS		Filing Date	November 4, 2003	
STA	LEMENT E	BY APPLIC	CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet	32	of	56	Attorney Docket Number	ISIS-5325	

	NON PATENT LITERATURE DOCUMENTS
62	Horton, N. C. et al., "The Structure of an RNA/DNA Hybrid: A Substrate of the Ribonuclease Activity of HIV-1 Reverse Transcriptase," J. Mol. Biol., 1996, 264, 521-533
62	Huang, L. et al., "Oligonucleotide conjugates of Eu(III) tetraazamacrocycles with pendent alcohol and amide groups promote sequence-specific RNA cleavage," J Biol Inorg. Chem (2000) 5:85-92.
62	Huh, N. et al., "Design, Synthesis, and Evaluation of Mitomycin-Tethered Phosphorothioate Oligodeoxynucleotides," Bioconiugate Chem. (1996) 7:659-669.
62	Hunter, "Genetics: a touch of elegance with RNAi," Current Biology, Current Science (1999) 9(12): R440-R442
62	Hyrup, B. And Nielsen, P., "Peptide Nucleic Acids (PNA): Synthesis, Properties and Potential Applications", Bioorganic & Med. Chem., 1996, 4, 5-23
63	Ikehara, et al, "Studies of Nucleosides and Nucleotides-LXV' Purine Cyclonucleosides-26 A Versatile Method for the Synthesis of Purine O-Cyclo-Bucleosides. The First Synthesis of 8,2'Anhydro-8-Oxy 9-B-D-Arabinofuranosylguanine," Tetrahedron, 1975, 31, 1369-1372
63	Ikehara, et al, "Studies of Nucleosides and Nucleotides-LXXXVII. 1, Purine Cyclonucleosides. XLII. Synthesis of 2'deoxy-2'fluorofunaosine," Chem. And Pharm. Bull., 1981, 29, 1034-1038.
63	2 Ikehara, et al. "Purine cyclonucleosides. (43). Synthesis and properties of 2'halogen-2'deoxyguanosines 1," Chem and Pharm Bull., 1981, 29, 3281-3285
63	3 Ikehara, et al., "A Linear Relationship Between Electronegativity of 2'-Substituents and Conformation of Adenine Nucleosides," Tetrahedron Letters, 1979, 42, 4073-4076
63	Ikehara, et al., "Improved Synthesis of 2'-fluoro-2'deoxyadenosine and Synthesis and Carbon-13 NMR Spectrum of its 3',5'-cyclic Phosphate Derivative," Nucleosides & Nucleotides, 1983, 2, 373-385
63	Ikehara, et al., "Polynucleotides. L. synthesis and properties of poly (2'chloro-2'-deoxyadenylic acid) and poly (2'-bromo-2'-deoxyadenylic acid)", Nucleic Acids Res., 1978, 4, 4249-4260
63	Ikehara, et al., "Polynucleotides. LII. Synthesis and properties of poly (2'-deox-2'-fluoroadenylic acid)," Nucleic Acids Research, 1978, 5, 1877-1887
63	7 Ikehara, et al., "Polynucleotides. LVI. Synthesis and Properties of Poly(2'-deoxy-2'-fluoroinosinic Acid)", Nucleic Acids Res., 1978, 5, 3315-3324
63	8 Ikehara, et al., "Purine 8-Cyclonucleosides," Accts. Chem Res., 1969, 2, 47-53

Examiner	Date	
Signature	Considered	

	0.1.67.1.6.4440/PT0			Complete if Known		
Substitute for 1	1449/PTO			Application Number	10/701,007	
		I DISCLOS		Filing Date	November 4, 2003	
STA <sup>-</sup>	TEMENT E	BY APPLIC	CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
	(use as many she	eets as necessary)		Examiner Name	Jane J. Zara	
Sheet 33 of 56		Attorney Docket Number	ISIS-5325			

	NON PATENT LITERATURE DOCUMENTS
639	Ikehara, et al., "Studies of Nucleosides and Nucleotides-LXXIV1 Purine Cyclonucleosides34 A New Method for the Synthesis of 2'-substituted 2'-deoxyadenosines," Tetrahedron, 1978, 34, 1133-1138
640	Ikehara, et al., "Studies of Nucleosides and Nucleotides-LXXXII. 1 Cyclonucleosides. (39). 2 Synthesis and properties of 2'halogen-2'-deoxyadenosines," Chem. Pharm. Bull., 1978, 26, 2449-2453
641	Ikehara, M., " 2'-substituted 2'-deoxypurineucleotides their conformation and properties," Heterocycles, 1984, 21(1), 75-90
642	Imazawa, et al., "Nucleosides and nucleotides. XII.1) Synthesis and properties of 2'-deoxy-2'-mercaptouridine and its derivates", Chem. Pharm. Bull., 1975, 23, 604-610
643	Inoue et al., "Sequence dependent hydrolysis of RNA using modified oligonucleotide splints and Rnase H", FEBS Lett., 1987, 215(2), 327-330
644	Inoue, et al., "Synthesis and hybridization studies on two complementary nona(2'-O-methyl) ribonucleotides", Nucleic Acid Res., 1987, 15, 6131-6148
645	International Search Report dated March 24, 2005 for International Application No. PCT/US03/35088
646	International Search Report dated November 18, 2004 for International Application No. PCT/US03/29294
647	Jacobson, K.A. et al., "Methanocarba Analogues of Purine Nucleosides as Potent and Selective Adenosine Receptor Agonists," J. Med. Chem., 2000, 43(11), 2196-2203
648	Jäger, A. et al., "Oligonucleotide N-alkylphosphoramidates: Synthesis and binding to polynucleotides", Biochemistry 1988, 27, 7237-7246
649	Janik, B., et al., "Synthesis and Properties of Poly 2'-Fluoro-2'-Deoxyuridylic Acid," Biochem. Biophys. Res. Comm., 1972, 46(3), 1153-1160
650	Jarvi, et al., "Synthesis and biological evaluation of dideoxunucleosides containing a difluoromethylene unit", Nucleosides & Nucleotides, 1989, 8, 1111-1114
651	Jaschke, A. et al., "Synthesis and properties of oligodeoxyribonucleotide-polyethyleneg lycol conjugates," Nucleic Acids Res. (1994) 22(22):4810-4817.
652	Jayaraman, et al., "Selective Inhibition of Escherichia Coli Protein Synthesis and Growth by Nonionic Oligonucleotides Complementary to the 3' end of 16S rRNA", Proc. Natl. Acad. Sci. USA 1981, 78(3), 1537-1541

Examiner	Date	
Signature	Considered	

	Out of the to for AAAO/DTO			Complete if Known		
Substitute for 1449/PTO				Application Number	10/701,007	
	RMATION			Filing Date	November 4, 2003	
STA	LEMENT E	BY APPLIC	ANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Jane J. Zara	
Sheet	34	of	56	Attorney Docket Number	ISIS-5325	

	NON PATENT LITERATURE DOCUMENTS
653	Jen et al., "Suppression of Gene Expression by Targeted Disruption of Messenger RNA: Available Options and Current Strategies," Stem Cells, 2000, 18, 307-319
654	Jones, et al., "4'-substituted nucleosides. 5. hydroxymethylation of nucleoside 5'-aldehydes", J. Org. Chem., 1979, 44, 1309-1317
655	Jones, et al., "Transient protection: Efficient one-flask synthesis of protected deoxynucleosides", J. Am. Chem. Soc., 1982, 104, 1316-1319
656	Jones, L.J. et al., "RNA Quantitation by Fluorescence-Based Solution Assay: RiboGreen Reagent Characterization," Anal. Biochem., 1998, 265, 368-374
657	Jones, S.S. et al., "Migration of t-Butyldimethylsilyl Protecting Groups," J.C.S. Perkin 1, 1979, 2762-2764
658	Jorgensen. R. A. et al., "Chalcone synthase cosuppression phenotypes in petunia flowers: comparison of sense vs. antisense constructs and single-copy vs. complex T-DNA sequences," Plant Mol. Biol., 1996, 31(5), 957-973
659	Juby, C. D. et al., "Facile Preparation of 3'0ligonucleotide-Peptide Conjugates," Tetrahedron Letters (1991) 32(7):879-882.
660	Jungblut, P.R., et al., "Proteomics in human disease: cancer, heart and infectious diseases," Electrophoresis, 1999, 20, 2100-2110
661	Jurecic, R., et al., "Long-distance DD-PCR and cDNA microarrays," Curr. Opin. Mocrobiol., 2000, 3, 316-321
662	Kabanov, A.V.,"A new class of antivirals: antisense olgonucleotides combined with a hydrophobic substituent effectively inhibit influenza virus reproduction and synthesis of virus-specific proteins in MDCK cells", FEBS Letts., 1990, 259, 327-330
663	Kadonaga, J.T. and Tjian, R.,"Affinity purification of sequence-specific DNA binding proteins", Proc. Natl. Acad. Sci. USA, 1986, 83, 5889-5893
664	Kadonaga, J.T., "Purification of Sequence-Specific Binding Proteins b DNA Affinity Chromatography", Methods in Enzymology, 1991, 208, 10-23
665	Kasher, et al., "Rapid Enrichment of HeLa Trancription Factors IIIB and IIIC by Using Affinity Chromatography Based on Avidin-Biotin Interactions", Mol. And Cell. Biol., 1986, 6, 3117-3127
666	Kawaguchi, et al., "Purification of DNA-binding transcription factors by their selective adsorption of the affinity atex particles", Nucleic Acids Research, 1989, 17, 6229-6240

Examiner	Date	
Signature	Considered	

		Complete if Known			
Substitute for 1449/PTO				Application Number	10/701,007
INFORMATION DISCLOSURE				Filing Date	November 4, 2003
STATEMENT BY APPLICANT		First Named Inventor	Charles Allerson		
				Art Unit	1635
(use as many sheets as necessary)				Examiner Name	Jane J. Zara
Sheet	35	of	56	Attorney Docket Number	ISIS-5325

	NON PATENT LITERATURE DOCUMENTS			
667	Kawasaki, et al., "Synthesis and Biophysical Studies of 2'-dRIBO-2'-F Modified Oligonucleotides", Conf. on Nucleic Acid Therapeutics, Clearwater, FL, Jan. 13-16, 1991, 10 pages			
668	Kawasaki, et al., "Uniformly Modified 2'-Deoxy-2'-fluoro Phosphorothioate Oligonucleotides as Nuclease-Resistant Antisense Compounds with High Affinity and Specificity for RNA Targets", J. Med. Chem., 1993, 36, 831-841			
669	Kawasaki, H/ et al., "Hesl is a target of MicroRNA-23 during retinoic-acid-induced neuronal differentation of NT2 cells," Nature (2003) 423: 838-842			
670	Kennedy, "Hydrophobic Chromatography", Methods in Enzymology, 1990, 182, 339-343			
671	Khurshid et al., "The unique conformational stability of poly 2'-O-Ethyladenylic Acid," FEBS Letters, 1972, 28(1), 25			
672	Khvorova, A. et al., "Functional siRNAs Exhibit Strand Bias," Cell, 2003, 115(2), 209-216			
673	Kiaris, H. et al., "Antagonists of Growth Hormone-Releasing Hormone Inhibit the Growth of U-87MG Human Gliobastoma in Nude mice," Neoplasia, 2000, 2(3), 242-250			
674	Kielanowska et al., "Preparation and properties of poly 2'-O-ethylcytidylic acid," Nucl. Acids Res., 1976, 3(3), 817-824			
675	Kimura-Harada, "5-methyl-2-thiouridine: A new sulfur-containing minor constituent from rat liver glutamic acid and lysine tRNAs," FEBS Lett., 1971, 13, 335-338			
676	Kingston, R.E. et al., "Calcium Phosphate Transfection", Current Protocols in Neuroscience, 1997, Supplement 1, A.1C.1 – A.1C.8			
677	Klopffer, A.E. et al., "Synthesis of 2'-Aminoalkyl-Substituted Fluorinated Nucleobases and Their Influence on the Kinetic Properties of Hammerhead Ribozymes," ChemBioChem (2004) 5: 707-716			
678	Klopffer, A.E. et al., "The effect of universal fluorinated nucleobases on the catalytic activity of ribozymes," Nucleosides Nucleotides Nucleic Acids (2003) 22(5-8): 1347-1350			
679	Knecht, D., "Application of Antisense RNA to the Study of the Cytoskeleton: Background, Principles, and a Summary of Results Obtained with Myosin Heavy Chain", Cell Motil. Cytoskel., 1989, 14, 92-102			
680	Knochbin et al., "An antisense RNA involved in p53 mRNA maturation in murine erythroleukemia cells induced to differentiate", EMBO J., 1989, 8, 4107-4114			
681	Knorre, et al., "Complementary-Addressed Sequence-Specific Modification of Nucleic Acids", Progress in Nucleic Acid Research and Molecular Biology 1985, 32, 291-321			
aminer nature	Date Considered			

0.1.111.4.6.4440/DT0		Complete if Known			
Substitute for 1449/PTO				Application Number	10/701,007
INFORMATION DISCLOSURE				Filing Date	November 4, 2003
STATEMENT BY APPLICANT		First Named Inventor	Charles Allerson		
				Art Unit	1635
(use as many sheets as necessary)				Examiner Name	Jane J. Zara
Sheet	36	of	56	Attorney Docket Number	ISIS-5325

	NON PATENT LITERATURE DOCUMENTS					
682	Koizumi, M. et al., "Design of RNA enzymes distinguishing a single base mutation in RNA," Nucleic Acids Research, 1989, 17, 7059-7071					
683	Koole, et al., "Synthesis of phosphate-methylated DNA fragments using 9-fluorenylmethoxycarbonyl as transient base protecting group", J. Org. Chem., 1989, 54, 1657-1664					
684	Koshkin, A.A., et al., "LNA (locked nucleic acid): an RNA mimic forming exceedingly stable LNA:LNA duplexes," J. Am. Chem. Soc., 1998, 120, 13252-13253					
685	Koshkin, A.A., et al., "LNA (locked nucleic acids): synthesis of the adenine, cytosine, guanine, 5-methylcytosine, thymine and uracil bicyclonucleoside monomers, oligomerisation, and unprecedented nucleic acid recognition," Tetrahedron, 1998, 54, 3607-3630					
686	Kraynack, B.A. et al., "Small interfering RNAs containing full 2'-O-methylribonucleotide-modified sense strands display Argonaute2/elF2C2-dependent activity," RNA, 2006, 12, 163-176					
687	Krieg, A. M. et al., "Uptake of Oligodeoxyribonucleotides by Lymphoid Cells Is Heterogeneous and Inducible," Antisense Research and Development (1991) 1:161-171.					
688	Krinke, L. et al., "RNase III-dependent hybrolysis of ÿcII-O gene mRNA mediated by ÿ OOP antisense RNA", Genes & Devel., 1990, 4, 2223-2233					
689	Kroschwitz, J.I. (Ed.), The Concise Encyclopedia of Polymer Science and Engineering, John Wiley & Sons, 1990, 858-859					
690	Krug, A., et al., "Synthesis of oligonucleotide probes containing 2'-deoxy-2'-fluoronucleosides for cleavage of RNA by RNase H," Biomed. Biochem. Acta, 1990, 49, 161-166					
691	Krug, A., et al., "The behaviour of 2'-deoxy-2'-fluorouridine incorporated into oligonucleotides by the phosphoramidite approach," Nucleosides & Nucleotides, 1989, 8(8), 1473-1483					
692	Krystal et al., "N-myc mRNA Forms an RNA-RNA Duplex with Endogenous Antisense Transcripts", Mol. And Cell. Biol., 1990, 10, 4180-4191					
693	Kuijpers, W. H. A. et al., "Specific Recognition of Antibody-Oligonucleotide Conjugates by Radiolabeled Antisense Nucleotides: A Novel Approach for Two-Step Radioimmunotherapy of Cancer," Bioconjugate Chem. (1993) 4(1):94-102.					
694	Kuimelis, "Synthesis of oligodeoxynucleotides containing 2-thiopyrimidine residuesa new protection scheme," Nucleic Acids Res. 1994, 22(8), 1429-1436					
695	Kumar et al., "Antisense RNA: function and fate of duplex RNA in cells of higher eukaryotes," Microbiology and Molecular Biology Reviews (1998) 62(4): 1415-1434					

Examiner	Date	
Signature	Considered	

Substitute for 1449/PTO				Complete if Known		
				Application Number	10/701,007	
		DISCLOS		Filing Date	November 4, 2003	
STA	LEMENT E	BY APPLIC	CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Jane J. Zara	
Sheet	37	of	56	Attorney Docket Number	ISIS-5325	

	NON PATENT LITERATURE DOCUMENTS	
696	Kumar, R., et al., "The first analogues of LNA (locked nucleic acids): phosphorothioate-LNA and 2'-thio-LNA," Bioorg. Med. Chem. Lett., 1998, 8, 2219-2222	
697	Kurchavov, N.A., et al., "A new phosphoramidite reagent for the incorporation of diazaphenoxazinone nucleoside with enhanced base-pairing properties into oligodeoxynucleotides," Nucleosides and Nucleotides, 1997, 16, 1837-1846	
698	Kurreck, J., "Antisense technologies, Improvement through novel chemical modifications," Eur. J. Biochem., 2003, 270(8), 1628-1644	
699	Kusmierek et al., "Alkyation of cytidine-5'-phosphate: Mechanisms of alkylation, influence of O'-alkylation on susceptibility of pyrimidine nucleotides to some nucleolytic enzymes, and synthesis of 2'-O-alkyl polynucleotides," ACTA Biochim. Polonica, 1973, 20(4), 365-381	
700	Lacerra, G., et al., "Restoration of hemoglobin a synthesis in erythroid cells from peripheral blood of thalassemic patients," Proc. Natl. Acad. Sci. USA, August 15, 2000, 97(17), 9591-9596	
701	Lai J. S. et al., "Fluorinated DNA Bases as Probes of Electrostatic Effects in DNA Base Stacking," Angew. Chem. Int. Ed. (2003) 42: 5973-5977	
702	Lai, J. S. et al., "Selective Pairing of Polyfluorinated DNA Bases," J. Am. Chem. Soc. (2004) 126(10): 3040-3041	
703	Lane, A. N. et al., "NMR Assignments and Solution Conformation of the DNA-RNA Hybrid Duplex d(GTGAACTT)-r(AAGUUCAC)," Eur. J. Biochem., 1993, 215, 297-306	
704	Larson, E.J., et al., "Rapid DNA fingerprinting of pathogens by flow cytometry," Cytometry, 2000, 41, 203-208	
705	Larsson, M., et al., "High-throughput protein expression of cDNA products as a tool in functional genomics," J. Biotechnol., 2000, 80, 143-157	
706	Le Doan et al., "Sequence-Targeted Chemical Modifications of Nucleic Acids by Complementary Oligonucleotides Covalently Linked to Porphyrins", Nucleic Acid Research, 1987, 15, 8643-8659	
707	Lee, R.C. et al., "The C. elegans heterochronic gene lin-4 encodes small RNAs with antisense complementarity to lin-14," Cell, 1993, 75(5), 843-854	
708	Lee, K. et al., "Ring-Constrained (N)-Methanocarba Nucleosides as Adenosine Receptor Agonists: Independent 5'-Uronamide and 2'-Deoxy Modifications," Bioorganic & Medicinal Chemistry Letters, 2001, 11(10), 1333-1337	
709	Lee, Y. et al., "MicroRNA maturation: stepwise processing and subcellular localization," EMBO J. (2002) 21(17): 4663-4670	

Examiner	Date	
Signature	Considered	

Substitute for 1449/PTO				Complete if Known		
				Application Number	10/701,007	
		I DISCLOS		Filing Date	November 4, 2003	
STA <sup>-</sup>	STATEMENT BY APPLICANT			First Named Inventor	Charles Allerson	
				Art Unit	1635	
	(use as many she	eets as necessary)		Examiner Name	Jane J. Zara	
Sheet	38	of	56	Attorney Docket Number	ISIS-5325	

	NON PATENT LITERATURE DOCUMENTS
710	Lee, Y. et al., "The nuclearRNase III Drosha initiates microRNA processing," Nature (2003) 425: 415-419
711	Leeds, J.M. et al., "Pharmacokinetic Properties of Phosphorothioate Oligonucleotides," Nucleosides Nucleotides, 1997, 16(7-9), 1689-1693
712	Lengyel, P., "Double-stranded RNA and interferon action," J. Interferon Res., 1987, 7, 511-519
713	Lesnik, E.A. et al., "Relative thermodynamic stability of DNA, RNA, and DNA:RNA hybrid duplexes: relationship with base composition and structure," Biochemistry, 1995, 34, 10807-10815
714	Letsinger et al., "Effects of Pendant Groups at Phosphorus on Binding Properties of D-ApA Analogues", Nucleic Acids Research, 1986, 14, 3487-3499
715	Letsinger, R.L. et al., "Cholesteryl-conjugated oligonucleotides: Synthesis, properties and activity as inhibitors of replication of human immunodeficiency virus in cell culture," Proc. Natl. Acad. Sci.,1989, 86, 6553-6556
716	Lewis, D.L. et al., "Efficient delivery of siRNA for inhibition of gene expression in postnatal mice," Nature Genetics, 2002, 32, 107-108
717	Li, S. et al., "Folate-Mediated Targeting of Antisense Oligodeoxynucleotides to Ovarian Cancer Cells," Pharm. Res. (1998) 15(10):1540-1545.
718	Liao, "A pyrimidine-guanine sequence-specific ribonuclease from Rana catesbeiana (bullfrog) oocytes", Nucl. Acids Res., 1992, 20, 1371-1377
719	Lima, W. F. et al., "Highly efficient endonucleolytic cleavage of RNA by a CyszHisz zinc-finger peptide," Proc. Natl. Acad. Sci. USA (1999) 96:10010-10015.
720	Lima, W.F. et al., "Binding affinity and specificity of Escherichia coli RNase H1: impact on the kinetics of catalysis of antisense oligonucleotide-RNA hybrids," Biochemistry, Vol. 36, pages 390-398 (1997)
721	Limbach, P.A. et al., "Summary: the modified nucleosides of RNA," Nucleic Acids Res., 1994, 22(12), 2183-2196
722	Lin, KY. et al., "A Cytosine Analogue Capable of Clamp-Like Binding to a Guanine in Helical Nucleic Acids," J. Am. Chem. Soc., 1998, 120(33), 8531-8532
723	Lin, KY. et al., "Tricyclic 2'-Deoxycytidine Analogs: Synthesis and Incorporation into Oligodeoxynucleotides Which Have Enhanced Binding to Complementary RNA," J. Am. Chem. Soc., 1995, 117, 3873-3874

Examiner	Date	
Signature	Considered	

Substitute for 1449/PTO				Complete if Known		
				Application Number	10/701,007	
	RMATION			Filing Date	November 4, 2003	
STATEMENT BY APPLICANT				First Named Inventor	Charles Allerson	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Jane J. Zara	
Sheet	39	of	56	Attorney Docket Number	ISIS-5325	

	NON PATENT LITERATURE DOCUMENTS	
724	Lin, M. et al., "Inhibition of collagenase type I expression by psoralen antisense oligonucleotides in dermal fibroblasts," Faseb J. 1995, 9, 1371-1377	
725	Liu, H. et al."A Four Base Paired Genetic Helix with Expanded Size," Science (2003) 302; 868-871	
726	Liu, H. et al., "Toward a New Genetic System with Expanded Dimensions: Size-Expanded Analogues of Deoxyadenosine and Thymidine," J. Am Chem Soc. (2004) 126(4) 1102-1109	
727	Liu, K. et al., "Efficient Nuclear Delivery of Antisense Oligodeoxynucleotides and Selective Inhibition of CETP Expression by Apo E Peptide in a Human CETP-Stably Transfected CHO Cell Line," Arterioscler. Thromb. Vasc. Biol. (1999) 19:2207-2213.	
728	Lixin, R. et al., "Novel Properties of the Nucleolar Targeting Signal of Human Angiogenin," Biochem. Biophys. Res. Comm. (2001) 284:185-193.	
729	Loakes, D. et al., "The applications of universal DNA base analogues," Nucleic Acids Res., 2001, 29(12), 2437-2447	
730	Lohrmann et al.,"New Solid Supports for DNA Synthesis", DNA, 1984, 3, 122	
731	Lukhtanov, E. A. et al., "Direct, Solid Phase Assembly of Dihydropyrroloindole Peptides with Conjugated Oligonucleotides," Bioconjugate Chem. (1996) 7(5):564-567.	
732	Lund et al., "Assessment of methods for covalent binding of nucleic acids to magnetic beads, Dynabeads™, and the characteristics of the bound nucleic acids in hybridization reactions", Nucl. Acids Res., 1988, 16, 10861-10880	
733	Madden, S.L., et al., "Serial analysis of gene expression: from gene discovery to target identification," Drug Discov. Today, September 2000, 5(9), 415-425	
734	Mahato et al., "Modulation of gene expression by antisense and antigene oligodeoxynucleotides and small interfering RNA," Expert Opinion on Drug Delivery, Jan. 2005, 2(1), 3-28	
735	Manche et al., "Interactions between double-stranded RNA regulators and the protein kinase DAI," Mol. Cell Biol., 1992, 12(11), 5238-5248	
736	Maniak, M. et al., "Evidence for a feedback regulated back-up promoter which controls permanent expression of a Dictyostelium gene", Nucl. Acids Res., 1990, 18, 5375-5380	
737	Manoharan M. et al., "Cholic Acid-Oligonucliotide Conjugates for Antisense Applications", Bioorganic Med. Chem. Letts., 1994, 4, 1053-1060	
738	Manoharan M. et al., "Oligonucleotide Conjugates: Alteration of the Pharmacokinetic Properties of Antisense Agents", Nucleosides and Nucleotides, 1995, 14, 969-973	

Examiner	Date	
Signature	Considered	

Substitute for 1449/PTO				Complete if Known		
				Application Number	10/701,007	
	RMATION			Filing Date	November 4, 2003	
STATEMENT BY APPLICANT				First Named Inventor	Charles Allerson	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Jane J. Zara	
Sheet	40	of	56	Attorney Docket Number	ISIS-5325	

	NON PATENT LITERATURE DOCUMENTS								
739	Manoharan, M. et al., "Chemical Modifications to Improve Uptake and Bioavailability of Antisense Oligonucleotides", Annals NY Acad. Sciences, 1992, 660, 306-309								
740	Manoharan, M. et al., "Introduction of a Lipophilic Thioether Tether in the Minor Groove of Nucleic Acids for Antisense Applications," Bioorg. Med. Chem. Letts., 1993, 3, 2765-2770								
74	Manoharan, M. et al., "Novel Functionalization of the Sugar Moiety of Nucleic Acids for Multiple Labeling in the Minor Groove," Tetrahedron Letters (1991) 32(49):7171-7174.								
742	Manoharan, M. et al., "Lipidic Nucleic Acids", Tetrahedron Letts., 1995, 36, 3651-3654								
743	Manoharan, M., "2'-Carbohydrate modifications in antisense oligonucleotide therapy: importance of conformation, configuration and conjugation," Biochimica et Biophysica Acta, 1999, 1489, 117-130								
74-	Manoharan, M., "Designer Antisense Oligonucleotides: Conjugation Chemistry and Functionality Placement," Antisense Research and Applications, Crooke and Lebleu, eds., CRC Press Boca Raton. FL, 1993, Chapter 17, 303-349.								
745	Manoharan, M., "Oligonucleotide Conjugates as Potential Antisense Drugs with Improved Uptake, Biodistribution, Targeted Delivery and Mechanism of Action," Antisense & Nucleic Acid Drug Development (2002) 12:103-128.								
740	Manoharan, M., "Oligonucleotide Conjugates in Antisense Technology," Antisense Drug Technology, Principles, Strategies, and Applications, Crooke, S. T. ed., Marcel Dekker, New York, (2001) Chapter 16, 391-467.								
74	Manoharan, M., "RNA interference and chemically modified small interfering RNAs," Current Opinion in Chemical Biology, 2004, 8, 570-579								
748	Marcus-Sekura, "Comparative inhibition of chloramphenicol acetyltransferase gene expression by antisense oligonucleotide analogues having alkyl phosphotriester, methylphosphonate and phosphorothioate linkages", Nucleic Acids Res., 1987, 15, 5749-5763								
749	Marcus-Sekura, "Techniques for Using Antisense Oligodeoxyribonucleotides to Study Gene Expression", Anal. Biochemistry, 1988, 172, 289-295								
750	Markiewicz, et al., "Simultaneous Protection of 3'- and 5'-Hydroxyl Groups of Nucleosides", Nucleic Acid Chemistry, Part 3, pgs. 229-231, L.B. Townsend, et al., Eds., J. Wiley and Sons, New York, 1986, 229-231								
75	Maruenda, H. et al., "Antisense Sequence-Directed Cross-Linking of DNA Oligonucleotides by Mitomycin C," Bioconjugate Chem. (1996) 7(5):541-544.								
752	Maruenda, H. et al., "Antisense sequence-directed cross-linking of RNA oligonucleotides by mitomycin," Anti-Cancer Drug. Des. (1997) 12, 473-479								
xaminer	Date								

Signature

Considered

Substitute for 1449/PTO				Complete if Known		
				Application Number	10/701,007	
	RMATION			Filing Date	November 4, 2003	
STATEMENT BY APPLICANT				First Named Inventor	Charles Allerson	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Jane J. Zara	
Sheet	41	of	56	Attorney Docket Number	ISIS-5325	

	NON PATENT LITERATURE DOCUMENTS							
753	Marwick, C., "First "Antisense" Drug Will Treat CMV Retinitis," J. Am. Med. Assoc., 1998, 280(10), 871							
754	Maskos, U. And Southern, E.M., "Oligonucleotide hybridisations on glass supports: a novel linker for oligonucleotide synthesis and hybridisation properties of oligonucleotides synthesised in situ", Nucl. Acids. Res., 1992, 20, 1679-1684							
755	Matson, et al., "Biopolymer Synthesis on Polypropylene Supports", Anal. Biochem., 1994, 217, 306-310							
756	Matsukura, M. et al., "Phosphorothioate Analogs of Oligodeoxynucleotides: Inhibitors of Replication and Cytopathic Effects of Human Immunodeficiency Virus", Proc. Natl. Acad. Sci. USA, 1987, 84, 7706-7710							
757	Matteucci, M.D. et al., "Synthesis of Deoxyoligonucleotides on a Polymer Support," J. Am. Chem. Soc., 1981, 103(11), 3185-3191							
758	McBride, L.J. and Caruthers, M.H., "An Investigation of Several Deoxynucleoside Phosphoramidites Useful for Synthesizing Deoxyoligonucleotides", Tetrahedron Letters, 1983, 24, 245-248							
759	McCafferey, A.P. et al., "RNA interference in adult mice," Nature, 2002, 418, 38-39							
760	McIntyre, K.W. et al., "A Sense Phosphorothioate Oligonucleotide Directed to the Initiation Codon of Transcription Factor NF-kB p65 Causes Sequence-Specific Immune Stimulation," Antisense Res. Dev., 1993, 3, 309-322							
761	McQueen, C.A. et al., "Effect of Nalidixic Acid on DNA Repair in Rat Hepatocytes," Cell Biol. Toxicol., 1989, 5(2), 201-206							
762	Meegan, J.M. et al., "Double-Stranded Ribonuclease Coinduced with Interferon", Science, 1989, 244, 1089-1091							
763	Metelev, et al., Bioorg. & Med. Chem. Lett., 1994, 4(24), 2929-2934							
764	Meunier, L. et al., "The nuclear export signal-dependent localization of oligonucleopeptides enhances the inhibition of the protein expression from a gene transcribed in cytosol," Nucleic Acids Res. 1999, 27(13):2730-2736							
765	Meyer, et al., "Efficient, Specific Cross-Linking and Cleavage of DNA by Stable, Synthetic Complementary Oligodeoxynucleotides", J. Am. Chem. Soc. 1989, 111, 8517-8519							
766	Mili, S. et al., "Distinct RNP Complexes of Shuttling hnRNP Proteins with Pre-mRNA and rnRNA. Candidate Intermediates in Formation and Export of mRNA," Mol. Cell Biol. (2001) 21(21):7307-7319.							

Examiner	Date	
Signature	Considered	

0 L 11 L 1 AAA0/DT0				Complete if Known		
Substitute for 1	1449/P1O			Application Number	10/701,007	
		DISCLOS		Filing Date	November 4, 2003	
STA	STATEMENT BY APPLICANT			First Named Inventor	Charles Allerson	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Jane J. Zara	
Sheet 42 of 56		Attorney Docket Number	ISIS-5325			

	NON PATENT LITERATURE DOCUMENTS						
767	Miller, et al., "A New Approach to Chemotherapy Based on Molecular Biology and Nucleic Acid Chemistry: Matagen (Masking Tape for Gene Expression", Anti-Cancer Drug Design, 1987, 2, 117-128						
768	Miller, et al., "Biochemical and Biological Effects of Nonionic Nucleic Acid Methylphosphonates", Biochemistry 1981, 20, 1874-1880						
769	Miller, et al., "Nonionic nucleic acid analogues. Synthesis and characterization of dideoxyribonucleoside methylphosphonates", Biochemistry 1979, 18, 5134-5143						
770	Miller, et al., "Synthesis and properties of adenine and thymine nucleoside alkyl phosphotriesters, the neutral analogs of dinucleoside monophosphates", J. Am. Chem. Soc. 1971, 93, 6657-6664						
771	Milligan, "Current concepts in antisense drug design," J. Med. Chem., 1993, 36, 1923-1937						
772	Min, KL. et al., "Oligonucleotides comprised of alternating 2' -deoxy-2' -fluoro-beta-D-arabinonucleosides and D-2' -deoxyribonucleosides (2'F-ANA/DNA 'Altimers') induce efficient RNA cleavage mediated by RNase H," Bioorganic & Medicinal Chemistry Letters, September 2002, 12, 2651-2654						
773	Mishra et al., "Improved leishmanicidal effect of phosphorotioate antisense oligonucleotides by LDL-medicated delivery", Biochim. Biophys. Acta, 1995, 1264, 229-237						
774	Miura et al., "Fluorometric determination of total mRNA with oligo(dT) immobized on microtiter plates", Clin. Chem., 1996, 42(11), 1758-1764						
775	Monia, et al., "Antitumor activity of a phosphorothioate antisense oligodeoxynucleotide targeted against c-raf kinase", Nature Medicine, 1996, 2, 668-675						
776	Monia, et al., "Evaluation of 2'-Modified Oligonucleotides Containing 2'-Deoxy Gaps as Antisense Inhibitors of Gene Expression", J. Biol. Chem., 1993, 268, 14514-14522						
777	Monia, et al., "Selective Inhibition of Mutant Ha-ras mRNA Expression by Antisense Oligonucleotides", J. Biol. Chem., 1992, 267, 19954-19962						
778	Montgomery, M.K. et al., "RNA as a target of double-stranded RNA-mediated genetic interference in Caenorhabditis elegans," Proc. Natl. Acad. Sci. USA, 1998, 95(26), 15502-15507						
779	Moran, S. et al., "A thymidine triphosphate shape analog lacking watson-crick pairing ability is replicated with high sequence selectivity," Proc. Natl. Acad. Sci. USA (1997) 94, 10506-10511						
780	Moran, S. et al., "Difluorotoluene, a Nonpolar Isostere for Thymine, Codes Specifically and Efficiently for Adenine in DNA Replication," J Am Chem Soc. (1997) 119(8), 2056-2057						

Examiner	Date	
Signature	Considered	

0 L 111 L C 1110/DT0				Complete if Known		
Substitute for 1449/PTO				Application Number	10/701,007	
		I DISCLOS		Filing Date	November 4, 2003	
STA <sup>-</sup>	STATEMENT BY APPLICANT			First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet 43 of 56		Attorney Docket Number	ISIS-5325			

	NON PATENT LITERATURE DOCUMENTS						
781	Morita, K. et al., "2'-O,4'-C-Ethylene-Bridged Nucleic Acids (ENA): Highly Nuclease-Resistant and Thermodyamically Stable Oligonucleotides for Antisense Drug," Bioorganic & Medicinal Chemistry Letters, 2002, 12(1), 73-76						
782	Morita, K. et al., "Synthesis and Properties of 2'-0,4'-C-Ethylene-Bridged Nucleic Acids (ENA) as Effective Antisense Oligonucleotides," Bioorg. Med. Chem., 2003, 11, 2211-2226						
783	Moulds, C. et al., "Site and Mechanism of Antisense Inhibition by C-5 Propyne Oligonucleotides," Biochemistry, 1995, 34(15), 5044-5053						
784	Napoli, C. et al., "Introduction of a Chimeric Chalcone Synthase Gene into Petunia Results in Reversible Co-Suppression of Homologous Genes in trans," Plant Cell, 1990, 2(4), 279-289						
785	Narhi, et al., "Hydrophobic Interaction Chromatography in Alkaline pH", Anal. Biochem., 1989, 182, 266-270						
786	Nasevicius, A. et al., "Effective targeted gene 'knockdown' in zebrafish," Nature Genetics, 2000, 26, 216-220						
787	Nellen, W., C., "What makes an mRNA anti-sense-itive?", Curr. Opin. Cell. Biol., 1993, 18, 419-424						
788	Nellen, W., et al., "Mechanisms of gene regulation by endogenous and artificially introduced antisense RNA", Biochem., Soc. Trans., 1992, 20, 750-754						
789	NELSON, P. S. et al., "Bifunctional oligonucleotide probes synthesized using a novel CPG support are able to detect single base pair mutations," Nucleic Acids Res. (1989) 17(18):7187-7194						
790	Nestle, F.O. et al., "Cationic Lipid is not Required for Uptake and Selective Inhibitory Activity of ICAM-1 Phosphorothioate Antisense Oligonucleotides in Keratinocytes," J. Invest. Dermatol., 1994, 103, 569-575						
791	Nielsen et al., "Sequence-Selective Recognition of DNA by Strand Displacement with a Thymine-Substituted Polyamide", Science, 1991, 254, 1497-1500						
792	Nishikura, K. et al., "A Short Primer on RNAi: RNA-Directed RNA Polymerase Acts as a Key Catalyst," Cell, 2001, 107(4), 415-418						
793	Nitta, et al., "Purification and Some Properties of Ribonuclease from Xenopus laevis Eggs", Biol. Pharm. Bull. (Jpn.), 1993, 16, 353-356						
794	Noguchi, et al., "Characterization of an Antisense Inr Element in the eIF-2α Gene", J. Biol. Chem., 1994, 269, 29161-29167						

Examiner	Date	
Signature	Considered	

0 L 111 L C 1110/DT0				Complete if Known		
Substitute for 1449/PTO				Application Number	10/701,007	
		DISCLOS		Filing Date	November 4, 2003	
STA <sup>-</sup>	STATEMENT BY APPLICANT			First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet 44 of 56		Attorney Docket Number	ISIS-5325			

	NON PATENT LITERATURE DOCUMENTS						
795	Noyes, et al., "Nucleic Acid Hybridization Using DNA Covalently Coupled to Cellulose", Cell, 1975, 5, 301-310						
796	Nykänen, A. et al, "ATP Requirements and Small Interfering RNA Structure in the RNA Interference Pathway," Cell, 2001, 107, 309-321						
797	Oberhauser et al., "Effective incorporation of 2'-O-methyl-oligonucleotides into liposomes and enhanced cell association through modification with thiocholesterol", Nucl. Acids Res., 1992, 20(3), 533-538						
798	Ogilvie, K.K. et al., "The Use of Silyl Groups in Protecting the Hydroxyl Functions of Ribonucleosides," Tetrahedron Letters, 1974, 15(33), 2861-2863						
799	Ohtsuka et al., "Recognition By Restriction Endonuclease EcoRI of Deoxyoctanucleotides containing modified sugar moieties," Eur. J. Biochem., Mar. 1984, 447-450						
800	Ohtsuki, et al., "Isolation and purification of double-stranded ribonuclease from calf thymus", J. Biol. Chem., 1977, 252, 483-491						
801	Olie, R.A. et al., "Analysis of ribosyl-modified, mixed backbone analogs of a bcl-2/bcl-xL antisense oligonucleotide," Biochimica et Biophysica Acta, 1576 (2002), 101-109						
802	Olsen, D.B., et al., "Study of a Hammerhead Ribozyme Containing 2'-Modified Adenosine Residues," Biochemistry, 1991, 30:, 9735-9741						
803	O'Neill, B.M. et al., "A Highly Effective Nonpolar Isostere of Deoxyguanosine: Synthesis, Structure, Stacking, and Base Pairing," J. Org. Chem. (2002) 67(17):5869-5875						
804	Ørum, H. et al., "Locked nucleic acids: A promising molecular family for gene-function analysis and antisense drug development," Curr. Opin. Mol. Therap., 2001, 3(3), 239-243						
805	Outten, et al., "Synthetic 1-methoxybenzo[d]naphtho[1,2-b]pyran-6-one c-glycosides", J. Org. Chem. 1987, 52, 5064-5066						
806	Owen, et al., "Transcriptional activation of a conserved sequence element by ras requires a nuclear factor distinct from c-fos or c-jun", Proc. Natl. Acad. Sci USA, 1990, 87, 3866-3870						
807	Owen, G.R. et al., "4'-Substituted Nucleosides. 3. Synthesis of Some 4'-Fluorouridine Derivatives," J. Org. Chem., 1976, 41(18), 3010-3017						
808	Parker, J.S. et al., "Structure insights into mRNA recognition from a PIWI domain-siRNA guide complex," Nature, 2005, 434, 663-666						
809	Parkes, et al., "A short synthesis of 3'-cyano-3'-Deoxythymidine", Tetra. Lett., 1988, 29, 2995-2996						

Examiner	Date	
Signature	Considered	

0 L ("L L L AAAO/DTO				Complete if Known		
Substitute for 1449/PTO				Application Number	10/701,007	
		DISCLOS		Filing Date	November 4, 2003	
STATEMENT BY APPLICANT			CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet 45 of 56		Attorney Docket Number	ISIS-5325			

	NON PATENT LITERATURE DOCUMENTS						
810	Parr, W. et al., "Solid-Phase Peptide Synthesis on an Inorganic Matrix having Organic Groups on the Surface," Angew Chem. Internat. Edit, 1972, 11 (4), 314-315						
811	Patzel et al., "A Theoretical Approach to Select Effective Antisense Oligodeoxyribonucleotides at High Statistical Probability," Nucleic Acids Research (1999) pp. 4328-4334.						
812	Pease, et al., "Light-generated oligonucleotide arrays for rapid DNA sequence analysis", Proc. Natl. Acad. Sci. USA, 1994, 91, 5022-5026						
813	Petersen, M. et al., "The conformations of locked nucleic acids (LNA)," J. Mol. Recognit., 2000, 13, 44-53						
814	Petersheim, et al., "Base-Stacking and Base-Pairing contributions to helix stability: thermodynamics of double-helix formation with CCGG, CCGGp, CCGGAp, ACCGGp, CCGGUp, and ACCGGUp", Biochemistry, 1983, 22, 256-263						
815	Pichon, C. et al., "Intracellular Routing and Inhibitory Activity of Oligonucleopeptides Containing a KDEL Motif," Mol. Pharmacol. (1997) 51:431-438.						
816	Pieken, W.A. et al., "Kinetic Characterization of Ribonuclease-Resistant 2'-Modified Hammerhead Ribozymes," Science, 1991, 253, 314-317						
817	Pieken, W.A., et al., "Structure-Function Relationship of Hammerhead Ribozymes as Probed by 2'-Modifications," Nucleic Acids Symp Ser., 1991, 24, 51-53						
818	Pike et al., "Mixed Alkylation (Methylation and Ethylation) of Adenosine by Diazoethane in Aqueous 1,2-Dimethoxyethane," J. Org. Chem., 1974, 39(25), 3674-3676						
819	Pilet, J. et al., "Structural parameters of single and double helical polyribonucleotides," Biochem Biophys Res Commun, 1973, 52(2), 517-523						
820	Pitts, A.E. et al., "Inhibition of human telomerase by 2'-O-methyl-RNA," Proc. Natl. Acad. Sci. USA, 1998, 95, 11549-11554						
821	Pon, et al., "Derivatization of Controlled Pore Glass Beads for Solid Phase Oligonucleotide Synthesis", BioTech., 1988, 6, 768-773						
822	Poopeiko, N.E. et al., " <i>Xylo</i> -configured Oligonucleotides (XNA, Xylo Nucleic Acid): Synthesis of Conformationally Restricted Derivatives and Hybridization Towards DNA and RNA Complements," Biorganic & Medicinal Chemistry Letters 2003, vol. 13, pages 2285-2290						
823	Porta, H. et al., "An allosteric hammerhead ribozyme," Biotechnology (N.Y.), 1995, 13(2), 161-164						
824	Prakash, T. P. et al., Abstract of The 227th ACS National Meeting, Anaheim, CA, March 28-April 1, 2004						

Examiner	Date	
Signature	Considered	

0 L ("L L C 4440/DT0				Complete if Known		
Substitute for 1449/PTO				Application Number	10/701,007	
	RMATION			Filing Date	November 4, 2003	
STATEMENT BY APPLICANT			ANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Jane J. Zara	
Sheet	46	of	56	Attorney Docket Number	ISIS-5325	

	NON PATENT LITERATURE DOCUMENTS						
825	Prakash, T. P. et al., "Synthesis of Site-Specific Oligonucleotide-Polyamine Conjugates," Bioorg. Med. Chem. Lett. (1994) 4(14):1733-1738.						
826	Prashar, Y., et al., "A method for display of 3'-end fragments of restriction enzyme-digested cDnAs for analysis of differential gene expression," Methods Enzymol., 1999, 303, 258-272						
827	Prokipcak, et al., "Purification and Properties of a Protein that Binds to the C-terminal Coding Region of Human c-myc mRNA", J. Biol. Chem., 1994, 269, 9261-9269						
828	Puglisi, et al., "Absorbance melting curves of RNA", Methods in Enzymology, 1989, 180, 304-325						
829	Rajur, S. B. et al., "Covalent Protein-Oligonucleotide Conjugates for Efficient Delivery of Antisense Molecules," Bioconjugate Chem. (1997) 8(6):935-940.						
830	Rajwanshi, V.K., et al., "LNA stereoisomers: xylo-LNA (β-D-xylo configured locked nucleic acid) and α-L-ribo configured locked nucleic acid)," Chem. Commun., 1999, 1395-1396						
831	Ranganathan, "Modification of the 21-Position of Purine Nucleosides: Synthesis of 21-a-Substituted-21-Deoxyadenosine Analogs", Tetrahedron Letters, 1977, 15, 1291-1294						
832	Ransford et al., "2'-O-Ethyl Pyrimidine Nucleosides," J. Carbohydrates - Nucleosides - Nucleotides, 1974, 1(3), 275-278						
833	Rao, et al., "A Novel One-step Procedure for the Conversion of Thymidine into 2,3'-Anhydrothymidine", J. Chem. Soc. Chem. Commun., 1989, 997-998						
834	Rausch, J.W. et al., "Hydrolysis of RNA/DNA hybrids containing nonpolar pyrimidine isosteres defines regions essential for HIV type 1 polypurine tract selection," PNAS (2003) 100(20): 11279-11284						
835	Reddy, M.P. et al., "Fast Cleavage and Deprotection of Oligonucleotides," Tetrahedron Letters, 1994, 35(25), 4311-4314						
836	Reese, C.B. et al., "An Acetal Group Suitable for the Protection of 2'hydroxy Functions in Rapid Oligoribonucleotide Synthesis," Tetrahedron Letters, 1986, 27(20), 2291-2294						
837	Reese, C.B., et al., "4-(1,2,4-Triazol-1-yl)-and 4-(3-Nitro-1,2,4-triazol-1-yl)-1-(β-D-Arabinofuranosyl)cytosine(Ara-C)", J. Chem. Soc. Perkin Trans. I, 1982, pgs. 1171-1176						
838	Renneberg, D. et al. "Antisense properties of tricyclo-DNA," Nucleic Acids Res., 2002, 30(13), 2751-2757						
839	Renneberg, D., et al., "Watson—Crick base-pairing properties of tricycle-DNA," J. Am. Chem. Soc., 2002, 124, 5993-6002						

Examiner	Date	
Signature	Considered	

0.1.111.4.6.4440/DT0				Complete if Known		
Substitute for 1449/PTO				Application Number	10/701,007	
		DISCLOS		Filing Date	November 4, 2003	
STATEMENT BY APPLICANT			ANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Jane J. Zara	
Sheet	47	of	56	Attorney Docket Number	ISIS-5325	

	NON PATENT LITERATURE DOCUMENTS				
840	Revankar et al., "Synthesis and Antiviral/Antitumor of Certain 3-Seazaguanine Nucleosides and Nucleotides", J. Med. Chem. 1984, 24, 1389-1396				
841	Rhodes, J. et al., "Therapeutic potentiation of the immune system by costimulatory Schiffbaseforming drugs," Nature (1995) 377(6544):71-75.				
842	Robins, et al., "Nucleic acid related compounds. 41. Restricted furanose conformations of 3',5'-O(1,1,3,3-tetraisoprpyldisilox-1,3-diyl)nucleosides provide a convenient evaluation of anomeric configuration1,2", Can. J. Chem., 1983, 61, 1911-1920				
843	Robins, et al., "Nucleic Acid Related Compounds. 42. A General Procedure for the Efficient Deoxygenation of Secondary Alcohols. Regiospecific and Stereoselective Conversion of Ribonucleosides to 2'-Deoxynucleosides", J. Am. Chem. Soc., 1983, 105, 4059-4065				
844	Robins, et al., "Synthesis of 2'-Deoxytubercidin, 2'-Deoxyadenosine, and Related 2'-Deoxynucleosides via a Novel Direct Stereospecific Sodium Salt Glycosylation Procedure", J. Am. Chem. Soc., 1984, 106, 6379-6382				
845	Roelen et al., "Synthesis of Nucleic Acid Methylphos-Phonothioates", Nucleic Acids Research 1988, 16(15), 7633-7645				
846	Rottman et al., "Influence of 2'-O-Alkylation on the Structure of Single-Stranded Polynucleotides and the Stability of 2'-O-Alkylated Polynucleotide Complexes," Biochem., 1974, 13, 2762-2771				
847	Rottman, F. et al., "Polymers Containing 2'-O-Methylnucleotides. II. Synthesis of Heteropolymers," Biochem, 1969, 8(11), 4354-4361				
848	Rottman, F. et al., "Polynucleotides Containing 2'- 0-Methyladenosine. I. Synthesis by Polynucleotide Phosphorylase," Biochem, 1968, 7, 2634-2641				
849	Ruby, et al., "An Early Hierarchic Role of U1 Small Nuclear Ribonucleoprotein in Splicesome Assembly", Science, 1988, 242, 1028-1035				
850	Rump, E. T. et al., "Preparation of Conjugates of Oligodeoxynucleotides and Lipid Structures and Their interaction with Low-Density Lipoprotein," Bioconjugate Chem. (1998) 9(3):341-349.				
851	Ryan, et al., "Synthesis of 2-Thio-D-ribose and 2'-Thioadenosine Derivatives", J. Org. Chem., 1971, 36(18), 2646-2657				
852	Saison-Behmoaras, T., et al., "Short modified antisense oligonucleotides directed against Haras point mutation induce selective cleavage of the mRNA and inhibit T24 cells proliferation", EMBO, 1991, 10, 1111-1118				
853	Saito, H. And Richardson, C., "Processing of mRNA by Ribonuclease III Regulates Expression of Gene 1.2 of Bacteriophage T7", 1981, Cell, 27, 533-542				

Examiner	Date	
Signature	Considered	

0 L (1) L ( A440/DT0				Complete if Known		
Substitute for 1449/PTO				Application Number	10/701,007	
		DISCLOS		Filing Date	November 4, 2003	
STATEMENT BY APPLICANT			CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Jane J. Zara	
Sheet	48	of	56	Attorney Docket Number	ISIS-5325	

	NON PATENT LITERATURE DOCUMENTS						
854	Sambrook, et al., "Molecular Cloning. A Laboratory Manual", Cold Spring Harbor Laboratory Press, 1989, Vol. 2, pgs. 11.31-11.32						
855	San et al., "Safety and short term toxicity of a novel cationic lipid formulation for human gene therapy", Human Gene Therapy, 1993, 4, 781-788						
856	Sands, et al., 'Biodistribution and Metabolism of Internally 3H-Labeled Oligonucleotides. II. 3',5'-Blocked Oligonucleotides", Mol. Pharmacol., 1995, 47, 636-646						
857	Sanghvi, Y.S. et al., "Heterocyclic Base Modifications in Nucleic acids and their Applications in Antisense Oligonucleotides", Antisense Research and Applications, CRC Press, Boca Raton, Chapter 15, 1993, 273-288						
858	Scaringe, S.A. et al., "Novel RNA Synthesis Method Using 5'-O-Silyl-2'-O-orthoester Protecting Groups," J. Am. Chem. Soc., 1998, 120(45), 11820-11821						
859	Scaringe, S.A., "RNA Oligonucleotide Synthesis via 5'-Silyl-2'-Orthoester Chemistry," Methods, 2001, 23, 206-217						
860	Scaringe, S.A., Thesis entitled, "Design and Development of New Protecting Groups for RNA Synthesis," University of Colorado (1996)						
861	Scherer et al., "Approaches for the sequence-specific knockdown of mRNA," Nat. Biotechnol., 2003, 21(12), 1457-1465						
862	Schöning, KU., et al., "Chemical etiology of nucleic acid structure: the α-threofuranosyl-(3'→2') oligonucleotide system," Science, 2000, 290, 1347-1351						
863	Schott, "Template-Chromatographie An Stationar Gebundenen Oligonukleotiden", J. Chromatogr., 1975, 115, 461-476						
864	Schwartz, et al., "A microtransfection method using the luciferase-encoding reporter gene for the assay of human immunodeficiency virus LTR promoter activity", Gene, 1990, 88, 197-205						
865	Schwartz, M.E. et al., "Rapid Synthesis of Oligoribonucleotides Using 2'-O-(o-Nitrobenzyloxymethyl)-Protected Monomers," Bioorg. Med. Chem. Lett., 1992, 2(9), 1019-1024						
866	Schwarz, D.S. et al., "Asymmetry in the Assembly of the RNAi Enzyme Complex," Cell, 2003, 115(2), 199-208						
867	Searle, M. S. et al., "On the Stability of Nucleic Acid Structures in Solution: Enthalpy-Entropy Compensations, Internal Rotations and Reversibility," Nucl. Acids Res., 1993, 21(9), 2051-2056						

Examiner	Date	
Signature	Considered	

				Complete if Known		
Substitute for 1449/PTO				Application Number	10/701,007	
		DISCLOS		Filing Date	November 4, 2003	
STATEMENT BY APPLICANT			CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Jane J. Zara	
Sheet	49	of	56	Attorney Docket Number	ISIS-5325	

	NON PATENT LITERATURE DOCUMENTS						
868	Seela, et al., "Palindromic Octa- and Dodecanucleotides Containing 2'-Deoxytubercidin: Synthesis, Hairpin Formation, and Recognition by the Endodeoxyribonuclease", Biochemistry, 1987, 26, 2232-2238						
869	Seliger, H., et al., "Synthetic Oligonucleotides for Biomedical Applications," Nucleic Acids Symp Ser., 1991, 24:193-196						
870	Seliger, H., "Handelsubliche Polymere als Trager in der Oligonucleotidsynthese, 1", Die Makromolekulart Chemie, 1975, 176, 1611-1627						
871	Seliger, H., and Aumann, G., "Trager-Oigonucleotidsynthese an unvernetzten Copolymeren aus Vinylalkohol und N-Vinylpyrrolidon", Die Makromolekulare Chemie, 1975, 176, 609-627						
872	Seliger,H. And Aumann, G., "Oligonucleotide Synthesis on a Polymer Support Soluble in Water and Pyridine", Tetrahedron Letters, 1973, No. 31, 2911-2914						
873	Shea et al., "Synthesis, hybridization properties and antiviral activity of lipid- oligodeoxynucletide conjugates", Nucl. Acids Res., 1990, 18(13), 3777-3783						
874	Sheehan, D. et al., "Biochemical properties of phosphonoacetate and thiophosphonoactate oligodeoxyribonucleotides," Nucleic Acids Res., 2003, 31(14), 4109-4118						
875	Shi, Y., "Mammalian RNAi for the masses," Trends in Genetics (2003) 19(1): 9-12						
876	Shibahara, S. et al., "Inhibition of human immunodeficiency virus (HIV-1) replication by synthetic oligo-RNA derivatives," Nucl. Acids Res., 1989, 17(1), 239-252						
877	Shuman, S. et al., "Site-specific Interaction of Vaccinia Virus Topoisomerase I with Base and Sugar Moieties in Duplex DNA," J. Biol Chem, 1993, 268, 18943-18950						
878	Siddell, S.G., "RNA Hybridization to DNA Coupled with Cyanogen-Bromide-Activated Sephadex", Eur. J. Biochem., 1978, 92, 621-629						
879	Sigman, "Nuclease Activity of 1,10-Phenanthroline-Copper Ion", Acc. Chem. Res., 1986, 19, 180-186						
880	Sijen, T. et al., "On the role of RNA amplification in dsRNA-triggered gene silencing," Cell, Nov. 16, 2001, 107, 465-476						
881	Singer et al., "Alkylation of Ribose in RNA Reacted with Ethylnitrosourea at Neutrality," Biochem., 1976, 15(23), 5052						
882	Singh, S.K. et al., "LNA (locked nucleic acids): synthesis and high-affinity nucleic acid recognition," Chem. Commun., 1998, 4, 455-456						

Examiner	Date	
Signature	Considered	

Substitute for 1449/PTO				Complete if Known		
				Application Number	10/701,007	
		I DISCLOS		Filing Date	November 4, 2003	
STATEMENT BY APPLICANT			CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
	(use as many she	eets as necessary)		Examiner Name	Jane J. Zara	
Sheet	50	of	56	Attorney Docket Number	ISIS-5325	

	NON PATENT LITERATURE DOCUMENTS	
883	Singh, S.K., et al., "Synthesis of 2'-amino-LNA: a novel conformationally restricted high-affinity oligonucleotide analogue with a handle," J. Org. Chem., 1998, 63, 10035-10039	
884	Skorski, T. et al., "Antileukemia effect of c-myc N3'P5' phosphoramidate antisense oligonucleotides in vivo," Proc. Natl. Acad. Sci. USA, 1997, 94, 3966-3971	
885	Smith et al., "Antiviral effect of an oligo(nucleoside methylphosphonate) complementary to the splice junction of herpes simplex virus type 1 immediate early pre-mRNAs 4 and 5", Proc. Natl. Acad. Sci. USA, 1986, 83, 2787-2791	
886	Smith, et al., "The synthesis of oigonucleotides containing an aliphatic amino group at the 5' terminus: synthesis of fluorescent DNA primers for use in DNA sequence analysis", Nucl. Acids Res., 1985, 13, 2399-2412	
887	Smith, T.F. et al., "Comparison of Biosequences," Adv. Appl. Math., 1981, 2, 482-489	
888	Song, E. et al., "RNA interference targeting Fas protects mice from fulmiant hepatitis," Nature Med., 2003, 9(3), 347-351	
889	Song, JJ. et al., "The Crystal Structure of Argonaute and Its Implication for RISC Slicer Activity," Science, 2004, 305, 1434-1437	
890	Song, JJ. et al., "The crystal structure of the Argonaute2 PAZ domain reveals an RNA binding motif in RNAi effector complexes," Nature Struct. Biol., 2003, 10(12), 1026-1032	
891	Soutschek, J. et al., "Therapeutic silencing of a endogenous gene by systemic administration of modified siRNAs," Nature, 2004, 432(7014), 173-178	
892	Sproat, et al., "Highly Efficient Chemical Synthesis of 2'-O-methylioligoribunocleotides and Tetrabiotinylated Derivatives; Novel Probes That are Resistant to Degradation by RNA or DNA Specific Nucleases", Nucleic Acids Research, 1989, 17, 3373-3386	
893	Sproat, et al., "New synthetic routes to protected purine 2'-O-methylriboside-3'-O-phosphoramidites using a novel alkylation procedure", Nucleic Acids Research, 1990, 18, 41-49	
894	Steffens, R., et al., "168. Nucleic-acid analogs with constraint conformational flexibility in the sugar-phosphate backbone "tricycle-DNA'," Helv. Chim. Acta, 1997, 80, 2426-2439	
895	Steffens, R., et al., "Synthesis and thermodynamic and biophysical properties of tricycle-DNA," Am. Chem. Soc., 1999, 121(14), 3249-3255	
896	Stein, C.A. et al., 'Antisense Oligonucleotides as Therapeutic Agents - Is the Bullet Really Magical?", Science, 1993, 261, 1004-1012	

Examiner	Date	
Signature	Considered	

Substitute for 1449/PTO				Complete if Known		
				Application Number	10/701,007	
		DISCLOS		Filing Date	November 4, 2003	
STATEMENT BY APPLICANT			CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Jane J. Zara	
Sheet	51	of	56	Attorney Docket Number	ISIS-5325	

	NON PATENT LITERATURE DOCUMENTS						
897	Stein, et al., "Oligodeoxynucleotides as Inhibitors of Gene Expression: A Review", Cancer Research, 1988, 48, 2659-2668						
898	Stein, et al., "Physicochemical properties of phosphorothioate oligodeoxynucleotides", Nucleic Acids Research, 1988, 16, 3209-3221						
899	Stolt, P. And Zillig, W., "Antisense RNA mediates transcriptional processing in an archaebacterium, indicating a novel kind of RNase activity", Mol. Microbiol., 1993, 7, 875-882						
900	Strickland, et al., "Antisense RNA Directed Against the 3' Noncoding Region Prevents Dormant mRNA Activation in Mouse Oocytes", Science, 1988, 241, 680-684						
901	Struck, "Vaccine R&D Success Rates and Development Times," Nature Biotechnology, May 1996, 14, 591-593						
902	Stufkens, et al., "Dynamic Jahn-Teller Effect in the Excited States of SeCl62-, SeBr62-, TeCl62- and TeBr62-", Recueil des Travaux Chimiques des Pays-Bas 1970, 89, 1185-1201						
903	Stull, et al., "Antigene, Ribozyme and Aptamer Nucleic Acid Drugs: Progress and Prospects", Pharm. Res., 1995, Pharm. Rev., 12, 465-482						
904	Suciu et al., "Synthesis of 9-(2,5-dideoxy-β-D-glycero-pent-4-enofuranosyl)adenine", Carbohydrate Research, 1975, 44, 112-115						
905	Sutcliffe, J.G. et al., "TOGA: An automated parsing technology for analyzing expression of nearly all genes," PNAS, 2000, 97(5), 1976-1981						
906	Svinarchuk, F.P. et al., "Inhibition of HIV proliferation in MT-4 cells by antisense oligonucleotide conjugated to lipophilic groups," Biochimie, 1993, 75, 49-54						
907	Syvanen, et al., "Quantification of polymerase chain reaction products by affinity-based hybrid collection", Nucl. Acids Res., 1988, 16, 11327-11338						
908	Szyf, et al., "Growth Regulation of Mouse DNA Methyltransferase Gene Expression", J. Biol. Chem., 1991, 266, 10027-10030						
909	Tabara, H. et al., "RNAi in C. elegans: Soaking in the Genome Sequence," Science, 1998, 282(5388), 430-431						
910	Table listing related applications and office actions and rejections from those related applications						
911	Tamanini, F. et al., "The fragile X-related proteins FXRIP and FXRZP contain a functional nucleolar-targeting signal equivalent to the HIV-1 regulatory proteins," Hum. Mol. Genet. (2000) 9(10):1487-1493						

Examiner	Date	
Signature	Considered	

0 L 11 L 1 AAA0/DT0				Complete if Known		
Substitute for 1449/PTO				Application Number	10/701,007	
		DISCLOS		Filing Date	November 4, 2003	
STATEMENT BY APPLICANT			CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Jane J. Zara	
Sheet	52	of	56	Attorney Docket Number	ISIS-5325	

	NON PATENT LITERATURE DOCUMENTS						
912	Tang, XQ. et al., "2'-C-Branched Ribonucleosides: Synthesis of the Phosphoramidite Derivatives of 2'-C-Beta-Methylcytidine and Their Incorporation into Oligonucleotides," J. Org. Chem., 1999, 64(3), 747-754						
913	Tazawa et al., "A Novel Procedure for the Synthesis of 2'-O-Alkyl Nucleotides" Biochem., 1972, 11(26), 4931						
914	Thompson," Applications of Antisense and siRNAs During Preclinical Drug Development," DDT (2002) 7(17): 912-917						
915	Tidd, D.M. et al., "Evaluation of N-ras oncogene anti-sense, sense and nonsense sequence methylphosphonate oligonucleotide analogues," Anti-Cancer Drug Design, 1988, 3(2), 117-127						
916	Tijsterman, M. et al., "RNA Helicase MUT-14-Dependent Gene Silencing Triggered in C. elegans by Short Antisense RNAs," Science, 295(5555), 694-697						
917	Timmons, L. et al., "Ingestion of bacterially expressed dsRNAs can produce specific and potent genetic interference in Caenorhabditis elegans," Gene, 2001, 263(1-2), 103-112						
918	Timmons, L. et al., "Specific interference by ingested dsRNA," Nature, 1998, 395(6705), 854						
919	To, KY. "Identification of differential gene expression by high throughput analysis," Comb. Chem. & High Throughput Screen, 2000, 3, 235-241						
920	Tosquellas, G. et al., "The pro-oligonucleotide approach: solid phase synthesis and preliminary evaluation of model pro-dodecathymidylates," Nucleic Acids Research, 1998, 26(9), 2069-2074						
921	Tracewell et al., "In Vivo Modulation of Rat Cytochrome P450 1A1 by Double-Stranded Phosphorothioate Oligodeoxynucleotides, Toxicology and Applied Pharmacology, 1995, 135, 179-184						
922	Tseng et al., "Antisense Oligonucleotide Technology in the Development of Cancer Therapeutics", Cancer Gene Therapy, 1994, 1, 65-71						
923	Tuschl et al., "Targeted mRNA degradation by double-stranded RNA in vitro," Genes Dev, 1999, 13(24), 3191-3197						
924	Tuschl, T. et al., "Small interfering RNAs: a revolutionary tool for the analysis of gene function and gene therapy," Molecular Interventions, 2002, 2(3), 158-167						
925	U.S. Patent Application Serial No. 09/315,298 filed May 20, 1999, by Teng et al.						
926	U.S. Patent Application Serial No. 60/423,760 filed November 5, 2002, by Baker et al.						

Examiner	Date	
Signature	Considered	

Substitute for 1449/PTO				Complete if Known		
				Application Number	10/701,007	
		I DISCLOS		Filing Date	November 4, 2003	
STATEMENT BY APPLICANT			CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
	(use as many she	eets as necessary)		Examiner Name	Jane J. Zara	
Sheet	53	of	56	Attorney Docket Number	ISIS-5325	

NON PATENT LITERATURE DOCUMENTS						
927	Uhlmann et al., "Antisense Oligonucleotides: A New Therapeutic Principle", Chem. Rev., 1990, 90, 543					
928	Van der Krol, et al., "Modulation of Eukaryotic Gene Expression by Complementary RNA or DNA Sequences", BioTechniques, 1988, 6, 958-976					
929	Van Ness et al., "A versatile solid support system for oligodeoxynucleotide probe-based hybridization assays", Nucleic Acids Research, 1991, 19, 3345-3350					
930	Veronese et al., "Bioconjugation in pharmaceutical chemistry," II Farmaco, 1999, 54, 497-516					
931	Vickers, T.A. et al., "Efficient Reduction of Target RNAs by Small Interfering RNA and Rnase H-dependent Antisense Agents," J. Biol. Chem., 2003, 278(9), 7108-7118					
932	Volk et al., "An antisense transcript from the Xenopus laevis bFGF gene coding for an evolutionariy conserved 24 kd protein", EMBO J., 1989, 8, 2983-2988					
933	933 Wada, A. et al., "Nuclear export of actin: a novel mechanism regulating the subcellular localization of a major cytoskeletal protein," EMBO J. (1998) 17:1635-1641					
934	934 Wahlestedt, C., et al., "Potent and nontoxic antisense oligonucleotides containing locked nucleic acids," Proc. Natl. Acad. Sci. U.S.A., 2000, 97(10), 5633-5638					
935	Walder, et al., "Antisense DNA and RNA: Progress and Prospects", Genes & Development, 1988, 2, 502-504					
936	Walder, et al., "Role of RNase H in Hybrid-Arrested Translation by Antisense Oligonucleotides", Proc. Natl. Acad. Sci. USA 1988, 85, 5011-5015					
937	Wang, J., et al., "Syhthesis and binding property of an oligonucleotide containing tetrafluorophenoxazine," Tetrahedron Lett., 1998, 39, 8385-8388					
938	Wang, X. et al., "Modular Recognition of RNA by a Human Pumilio-Homology Domain," Cell (2002) 110:501-512.					
939	Wei, Z. et al., "Hybridization properties of oligodeoxynucleotide pairs bridged by polyarginine peptides," Nucleic Acids Res. (1996) 24(4):655-661.					
940	Wein, G. et al., "The 3'-UTR of the mRNA coding for the major protein kinase C substrate MARCKS contains a novel CU-rich element interacting with MRNA stabilizing factors HuD and HuR," Eur. 1. Biochem. (2003) 270:350-365.					
941	Wengel, J., et al., "LNA (locked nucleic acid)," Nucleosides, Nucleotides, 1999, 18(6 & 7), 1365-1370					

Examiner	Date	
Signature	Considered	

Substitute for 1449/PTO				Complete if Known		
				Application Number	10/701,007	
		DISCLOS		Filing Date	November 4, 2003	
STATEMENT BY APPLICANT			CANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet	54	of	56	Attorney Docket Number	ISIS-5325	

	NON PATENT LITERATURE DOCUMENTS				
942	Westermann et al., "Inhibition of expression of SV40 virus large T-antigen by antisense oligodeoxyribonucleotides", Biomed. B. Acta., 1989, 48, 85-93				
943	Wetlaufer et al., "Surfactant-Mediated Protein Hydrophobic-Interaction Chromatography", J. Chromatography, 1986, 359, 55-60				
944	Wianny et al., "Specific interference with gene function by double-stranded RNA in early mouse development," Nature Cell Biology (2000) 2: 70-75				
945	Wilds et al., "2'-Deoxy-2'-fluoro-B-D-arabinonucleosides and oligonucleotides (2'F-ANA): synthesis and phisicochemical studies," Nucleic Acids Res., 2000, 28, 3625-3635				
946	Wilds, C.J., et al., "Duplex recognition by oligonucleotides containing 2'-deoxy-2'-fluoro-D-arabinose and 2'-deoxy-2'-fluoro-D-ribose. Intermolecular 2'-OH-phosphate contacts versus sugar puckering in the stabilization of triple-helical complexes," Bioconjugate Chem., 1999, 10, 299-305				
947	Williams, D.M., et al., 'Properties of 2'-Fluorothymidine-Containing Oligonucleotides: Interaction with Restriction Endonuclease EcoRV," Biochemistry, 1991, 30, 4001-4009				
948	Wincott et al., "Synthesis, deprotection, analysis and purification of RNA and ribozymes," Nucl. Acids Res., 1995, 23(14), 2677-2684				
949	Wolfe, S., et al., "The guache effect. Some stereochemical consequences of adjacent electror pairs and polar bonds," Acc. Of Chem. Res., 1972, 5, 102-111				
950	Wouters, J. et al., "5-Substituted Pyrimidine 1,5-Anhydronhexitols: Conformational Analysis and Interaction with Viral Thymidine Kinase," Bioorg. Med. Chem. Lett., 1999, 9, 1563-1566				
951	Wright, P. et al., "Large Scale Synthesis of Oligonucleotides via Phosphoramidite Nucleosides and a High-loaded Polystyrene Support," Tetrahedron Lett., 1993, 34(21), 3373-3376				
952	Wu et al., "High Resolution Separation and Analysis of Biological Macromolecules", Methods in Enzymology, 1996, 270, 27-47				
953	Wu et al., "Purification and Properties of Drosophila Heat Shock Activator Protein", Science, 1987, 238, 1247-1253				
954	Wu, H. et al., "Identification and partial purification of human double strand RNase activity. A novel terminating mechanism for oligoribonucleotide antisense drugs," J. Biol. Chem, 1998, 273(5), 2532-2542				
955	Wu, H. et al., "Properties of Cloned and Expressed Human RNase H1," Journal of Biological Chemistry 1999, vol. 274, pages 28270-28278				

Examiner	Date	
Signature	Considered	

Substitute for 1449/PTO				Complete if Known		
				Application Number	10/701,007	
INFORMATION DISCLOSURE				Filing Date	November 4, 2003	
STATEMENT BY APPLICANT			CANT	First Named Inventor	Charles Allerson	
(use as many sheets as necessary)				Art Unit	1635	
				Examiner Name	Jane J. Zara	
Sheet	55	of	56	Attorney Docket Number	ISIS-5325	

	NON PATENT LITERATURE DOCUMENTS					
956	Wu, X., et al., "Base-pairing systems related to TNA: α-threofuranosyl oligonucleotides containing phosphoramidate linkages," Organic Lett., 2002, 4(8), 1279-1282					
957	Yang, Y. et al., "HIV-1 TAT-mediated protein transduction and subcellular localization using novel expression vectors," FEBS Letters (2002) 532, 36-44.					
958	Yashima et al., "High-performance affinity chromatography of oligonucleotides on nucleic acid analogue immobilized silica gel columns", J. Chromatog., 1992, 603, 111-119					
959	Yasuda et al., "Purification and characterization of a ribonuclease from human spleen", Eur. J. Biochem., 1990, 191, 523-529					
960	Yeung, et al., "Photoreactives and Thermal Properties of Psoralen Cross-Links", Biochemistry 1988, 27, 3204-3210					
961	Yu, D. et al., "Hybrid oligonucleotides: synthesis, biophysical properties, stability studies, and biological activity," Bioorganic and Medicinal Chemistry, 1996, 4(10), 1685-1692					
962	Yu, Y.T. et al., "A new method for detecting sites of 2'-O-methylation in RNA molecules," RNA, 1997, 3(3), 324-331					
963	Zamecnik, P.C. et al., "Inhibition of Rous sarcoma virus replication and cell transformation by a specific oligodeoxynucleotide," Proc. Natl. Acad. Sci. USA, 1978, 75(1), 280-284					
964	Zamore, P.D. et al., "Ancient Pathways Programmed by Small RNAs," Science, 2002, 296, 1265-1269					
965	Zamore, P.D. et al., "RNAi: Double-Stranded RNA Directs the ATP-Dependent Cleavage of mRNA at 21 to 23 Nucleotide Intervals," Cell, 2000, 101, 25-33					
966	Zanta, M. A. et al., "Gene delivery: A single nuclear localization signal peptide is sufficient to carry DNA to the cell nucleus," Proc. Natl. Acad. Sci. USA (1999) 96:91-96.					
967	Zarytova, et al., "Affinity Chromatography of DNA Fragments and P-Modified Oligonucleotides", Analyt. Biochem., 1990, 188, 214-218					
968	Zhang et al., "Single Processing Center Models for Human Dicer and Bacterial RNase III," Cell, 2004, 118, 57-68					
969	Zhang et al., "Targeted Gene Silencing by Small Interfering RNA-Based Knock-Down Technology," Current Pharmaceutical Biotechnology, 2004, 5, 1-7					
970	Zhang, H. et al., "Reduction of liver Fas expression by an antisense oligonucleotide protects mice from fuminant hepatitis," Nature Biotech., 2000, 18, 862-867					
971	Zhang, J., et al., "PowerBLAST: A new network BLAST application for interactive or automated sequence analysis and annotation," Genome Res., 1997, 7, 649-656					

0   11   1   1   1   1   1   1   1   1				Complete if Known		
Substitute for 1	Substitute for 1449/PTO			Application Number	10/701,007	
		DISCLOS		Filing Date	November 4, 2003	
STATEMENT BY APPLICANT			ANT	First Named Inventor	Charles Allerson	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Jane J. Zara	
Sheet	56	of	56	Attorney Docket Number	ISIS-5325	

NON PATENT LITERATURE DOCUMENTS					
972	Zhang, Z. et al., "Uptake of N-(4'-pyridoxyl)amines and release of amines by renal cells: A model for transporter-enhanced delivery of bioactive compounds," Proc. Natl. Acad. Sci. USA (1991) 88:10407-10410.				
973	Zhao, Q. et al., "Effect of Different Chemically Modified Oligodeoxynucleotides on Immune Stimulation," Biochemical Pharmacology, 1996, 51, 173-182				
974	Zhu, T. et al., "Oligonucleotide-Poly-L-omithine Conjugates: Binding to Complementary DNA and RNA." Antisense Res. Dm. 119931 3:265-275.				
975	Zmudzka, B. et al., "Poly 2'-0-methylcytidylic acid and the role of the 2'-hydroxyl in polynucleotide structure," Biochem Biophys Res Commun, 1969, 37(6), 895-901				
976	Zon, "Oligonucleotide Analogues as Potential Chemotherapy Agents", Pharm. Res., 1988, 5(9), 539-549				
977	Zon, "Synthesis of Backbone-Modified DNA Analogues for Biological Applications", J. Protein Chemistry, 1987, 6, 131-145				
978	Zuckermann, et al., "Efficient methods for attachment of thiol specific probes to the 3'-ends of synthetic oligodeoxyribonucleotides," Nucleic Acids Research, 1987, 15, 5305-5321				
979	Zuckermann, R. N. et al., "Site-Selective Cleavage of RNA by a Hybrid Enzyme," J. Am. Chem. SOC. (1988) 110:1614-1615.				

Examiner	/Jane Zara/	Date	07/15/2010
Signature		Considered	07/13/2010